## 10/628.999

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FILE 'MEDLINE, BIOSIS, EMBASE, CAPLUS' ENTERED AT 11:42:39 ON 15 SEP 2005
              E FALK RUDOLF/AU
             82 S E2-7
Ll
             5 S ASCULAI SAMUEL/AU
87 S L1 OR L2
L2
L3
            72 DUP REM L3 (15 DUPLICATES REMOVED)
L4
L5
        76962 S HYALURON?
            50 S L4 AND L5
L6
        2121801 S CANCER
L7
L8
         578462 S CHEMOTHERAP?
        290158 S ANTIOXIDANT
L9
          10501 S ANTI OXIDANT
L10
        559201 S VITAMIN
L11
         34839 S NSAID
52479 S NONSTEROIDAL
L12
L13
         61698 S NON STEROIDAL
L14
L15
           28 S L6 AND (L7 OR L8 OR L9 OR L10 OR L11 OR L12 OR L13 OR L14
            175 S L5 AND L12
L16
           166 S L16 NOT L15
L17
L18
           113 DUP REM L17 (53 DUPLICATES REMOVED)
L19
           487 S L5 AND L8
           485 S L19 NOT L15
L20
           343 DUP REM L20 (142 DUPLICATES REMOVED)
L21
L22
            23 S L21 AND (L9 OR L10 OR L11)
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L15 ANSWER 1 OF 28 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2001:380105 BIOSIS DOCUMENT NUMBER: PREV200100380105

DOCUMENT NUMBER: PREVZUUTUU380105

TITLE: Treatment of conditions and disease.

AUTHOR(S): Falk, Rudolf Edgar [Inventor, Reprint author];

Asculai, Samuel S. [Inventor]

CORPORATE SOURCE: Toronto, Canada

ASSIGNEE: Hyal Pharmaceutical Corporation, Mississauga,

Canada

PATENT INFORMATION: US 6194392 20010227

SOURCE: Official Gazette of the United States Patent and Trademark

Office Patents, (Feb. 27, 2001) Vol. 1243, No. 4. e-file.

CODEN: OGUPE7. ISSN: 0098-1133.

DOCUMENT TYPE: Patent LANGUAGE: English

ENTRY DATE: Entered STN: 8 Aug 2001

Last Updated on STN: 19 Feb 2002

AB A combination for administration to a mammal which combination employs a therapeutically effective amount of a medicinal and/or therapeutic agent to treat a disease or condition and an amount of hyaluronic acid and/or salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and subunits of hyaluronic acid sufficient to facilitate the agent's penetration through the tissue (including scar tissue) at the site to be treated, through the cell membranes into the individual cells to be treated.

L15 ANSWER 2 OF 28 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2001:273228 BIOSIS DOCUMENT NUMBER: PREV200100273228

TITLE: Use of hyaluronic acid and a NSAID for

the manufacture of a medicament for the treatment of

mucosal diseases.

AUTHOR(S): Asculai, Samuel S. [Inventor, Reprint author]; Falk,

Rudolf E. [Inventor]; Russell, Alan L. [Inventor]

CORPORATE SOURCE: Toronto, Canada

ASSIGNEE: SkyePharma PLC, London, UK

PATENT INFORMATION: US 6159955 20001212

SOURCE: Official Gazette of the United States Patent and Trademark

Office Patents, (Dec. 12, 2000) Vol. 1241, No. 2. e-file.

CODEN: OGUPE7. ISSN: 0098-1133.

DOCUMENT TYPE: Patent LANGUAGE: English

ENTRY DATE: Entered STN: 6 Jun 2001

Last Updated on STN: 19 Feb 2002

AB The use of an effective amount of a composition comprising an N.S.A.I.D.

and a form of hyaluronic acid selected from hyaluronic

acid, pharmaceutically acceptable salts thereof, fragments thereof and/or subunits thereof for mucous membrane trauma, disease, and/or pain relief.

L15 ANSWER 3 OF 28 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2001:253177 BIOSIS DOCUMENT NUMBER: PREV200100253177

TITLE: Formulations containing hyaluronic acid.
AUTHOR(S): Falk, Rudolf Edger [Inventor, Reprint au

HOR(S): Falk, Rudolf Edger [Inventor, Reprint author];
Asculai, Samuel Simon [Inventor]; Hochman, David

[Inventor]; Purschke, Don [Inventor]; Klein, Ehud Shmuel

[Inventor]; Harper, David William [Inventor]

CORPORATE SOURCE: Toronto, Canada

ASSIGNEE: Hyal Pharmaceutical Corporation, Mississauga,

Canada

PATENT INFORMATION: US 6136793 20001024

SOURCE: Official Gazette of the United States Patent and Trademark

Office Patents, (Oct. 24, 2000) Vol. 1239, No. 4. e-file.

CODEN: OGUPE7. ISSN: 0098-1133.

DOCUMENT TYPE: Patent LANGUAGE: English

ENTRY DATE: Entered STN: 23 May 2001

Last Updated on STN: 19 Feb 2002

AB A method of treating a disease or condition comprising administering topically to the skin or exposed tissue of a human, a dosage amount of a pharmaceutical composition, said dosage comprising a therapeutically effective amount of a drug to treat said disease or condition and a form of hyaluronic acid characterized in that the composition is immediately available to transport the drug percutaneously into the epidermis of the skin or exposed tissue to the site of trauma or pathology

of the disease or condition to be treated.

L15 ANSWER 4 OF 28 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

2001:204884 BIOSIS ACCESSION NUMBER: DOCUMENT NUMBER: PREV200100204884

TITLE: Formulations containing hyaluronic acid. Falk, Rudolf Edgar [Inventor, Reprint author]; AUTHOR(S):

Asculai, Samuel Simon [Inventor]; Klein, Ehud Shmuel [Inventor]; Harper, David W. [Inventor]; Hochman, David

[Inventor]; Purschke, Don [Inventor]

CORPORATE SOURCE: Toronto, Canada

ASSIGNEE: Hyal Pharmaceutical Corp., Canada

PATENT INFORMATION: US 6114314 20000905

Official Gazette of the United States Patent and Trademark SOURCE:

Office Patents, (Sep. 5, 2000) Vol. 1238, No. 1. e-file. CODEN: OGUPE7. ISSN: 0098-1133.

DOCUMENT TYPE: Patent LANGUAGE: English

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Entered STN: 25 Apr 2001 ENTRY DATE: Last Updated on STN: 18 Feb 2002

Topically applied transdermally quick penetrating (best targeting the epidermis and subsequently remaining there for a prolonged period of time) systemic independent acting, combinations and formulations which employ, combine, or incorporate a therapeutically effective non-toxic (to the patient) amount of a drug which inhibits prostaglandin synthesis together with an amount of hyaluronic acid and/or salts thereof (for example the sodium salt) and/or homologues, analogues, derivatives, complexes, esters, fragments, and/or sub units of hyaluronic acid to treat a disease and condition of the skin and exposed tissue for example, basal cell carcinoma, the precancerous, often recurrent, actinic keratoses lesions, fungal lesions, "liver" spots and like lesions (found for the most part in the epidermis), squamous cell tumours, metastatic cancer of the breast to the skin, primary and metastatic melanoma in the skin, genital warts cervical cancer, and HPV (Human Papilloma Virus) including HPV of the cervix, psoriasis (both plaque-type psoriasis and nail bed psoriasis), corns on the feet and hair loss on the head of pregnant women and remain in the skin for a prolonged period of time.

L15 ANSWER 5 OF 28 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2000:341677 BIOSIS DOCUMENT NUMBER: PREV200000341677

TITLE: Topical composition containing hyaluronic acid

and nsaids.

AUTHOR(S): Falk, Rudolf Edgar [Inventor, Reprint author];

Asculai, Samuel Simon [Inventor]

CORPORATE SOURCE: Toronto, Canada

ASSIGNEE: Hyal Pharmaceutical Corporation, Missisauga,

Canada

PATENT INFORMATION: US 6017900 20000125

SOURCE: Official Gazette of the United States Patent and Trademark

Office Patents, (Jan. 25, 2000) Vol. 1230, No. 4. e-file. CODEN: OGUPE7. ISSN: 0098-1133.

DOCUMENT TYPE: Patent LANGUAGE: English

Entered STN: 10 Aug 2000 ENTRY DATE:

Last Updated on STN: 7 Jan 2002

A pharmaceutical composition comprising a plurality of effective non-toxic dosage amounts of a composition for topical administration to the site of pathology or trauma of skin or exposed tissue of a human patient in need of treatment suffering from a disease or condition, each such dosage amount comprising a therapeutically effective non-toxic dosage amount of a drug for the treatment of the disease or condition of the skin or exposed tissue at the site of the pathology or trauma and an effective non-toxic dosage amount of hyaluronic acid or salts thereof or homologues, analogues, derivatives, complexes, esters, fragments, or sub-units of hyaluronic acid to transport the drug to the site of the pathology or trauma of the disease or condition.

L15 ANSWER 6 OF 28 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2000:289979 BIOSIS

DOCUMENT NUMBER: PREV200000289979

TITLE: Treatment of mucous membrane disease, trauma or condition

and for the relief of pain thereof.

AUTHOR(S): Asculai, Samuel Simon [Inventor, Reprint author]; Russell,

Alan Lawrence [Inventor]; Falk, Rudolf Edgar

[Inventor]

CORPORATE SOURCE: Mississauga, Canada

ASSIGNEE: Hyal Pharmaceutical Corporation

PATENT INFORMATION: US 5972906 19991026

Official Gazette of the United States Patent and Trademark SOURCE:

Office Patents, (Oct. 26, 1999) Vol. 1227, No. 4. e-file. CODEN: OGUPE7. ISSN: 0098-1133.

DOCUMENT TYPE: Patent LANGUAGE: English

Entered STN: 6 Jul 2000 ENTRY DATE:

Last Updated on STN: 7 Jan 2002

A method for the treatment of mucous membrane trauma disease or condition for the relief of pain associated therewith comprising administering topically an effective amount of a composition comprising an N.S.A.I.D. and a form of hyaluronic acid selected from hyaluronic

acid, pharmaceutically acceptable salts thereof, fragments thereof and/or

subunits thereof.

L15 ANSWER 7 OF 28 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 1999:494980 BIOSIS

DOCUMENT NUMBER: PREV199900494980

TITLE: Treatment of disease and conditions.

AUTHOR(S): Falk, Rudolf Edgar [Inventor, Reprint author];

Asculai, Samuel Simon [Inventor] CORPORATE SOURCE: University of Toronto, Toronto, Canada

ASSIGNEE: Hyal Pharmaceutical Corporation

PATENT INFORMATION: US 5914322 19990622

Official Gazette of the United States Patent and Trademark SOURCE:

Office Patents, (Jun. 22, 1999) Vol. 1223, No. 4. print. CODEN: OGUPE7. ISSN: 0098-1133.

DOCUMENT TYPE: Patent

LANGUAGE: English

ENTRY DATE: Entered STN: 16 Nov 1999

Last Updated on STN: 16 Nov 1999

L15 ANSWER 8 OF 28 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 1999:383189 BIOSIS

DOCUMENT NUMBER: PREV199900383189

TITLE: Topical composition containing hyaluronic acid

and NSAIDS.

AUTHOR(S): Falk, Rudolf Edgar [Inventor, Reprint author];

Asculai, Samuel Simon [Inventor]

CORPORATE SOURCE: University of Toronto, Toronto, Canada

ASSIGNEE: Hyal Pharmaceutical Corporation

PATENT INFORMATION: US 5910489 19990608

SOURCE: Official Gazette of the United States Patent and Trademark

Office Patents, (Jun.08, 1999) Vol. 1223, No. 2. print. CODEN: OGUPE7. ISSN: 0098-1133.

DOCUMENT TYPE: Patent LANGUAGE: English

ENTRY DATE: Entered STN: 13 Sep 1999

Last Updated on STN: 13 Sep 1999

L15 ANSWER 9 OF 28 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1998:789053 CAPLUS

DOCUMENT NUMBER: 130:29256

TITLE: Method of administration for a therapeutic agent

utilizing suitable forms of hyaluronic acid

and combinations with electroporation Falk, Rudolf E.; Asculai, Samuel S. Hyal Pharmaceutical Corp., Can.

PATENT ASSIGNEE(S):

PCT Int. Appl., 104 pp. SOURCE:

CODEN: PIXXD2 DOCUMENT TYPE: Patent

LANGUAGE: English FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

INVENTOR(S):

PAT	ENT	NO.			KIN	D	DATE		i	APPL	ICAT:	ION	NO.		D	ATE	
	9852 9852				A2 A3		1998: 1999:		1	WO 1	998-0	CA44	9		1	9980	511
	W:	AL, DK,	EE,	ES,	AU, FI,	AZ, GB,	BA, GE, LR,	BB, GH,	GM,	GW,	HU,	ID,	IL,	IS,	JP,	KE,	KG,

NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT,

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UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
CM, GA, GN, ML, MR, NE, SN, TD, TG
CA 2205692 AA 19981116 CA 1997-2205692 19970516
AU 9873287 A1 19981211 AU 1998-73287 19980511
PRIORITY APPLN. INFO.:
CA 1997-2205692 A 19970516
WO 1998-CA449 W 19980511
```

AB A method of administration for a therapeutic agent is disclosed which uses suitable forms of hyaluronic acid in combination with elec. assisted delivery methods, e.g. electrotransport or electroporation. The formulations of the invention include a therapeutic agent and sufficient hyaluronic acid to facilitate the therapeutic agent's penetration through the tissue (including scar tissue), at the site to be treated, through the cell membranes into the individual cells to be treated.

L15 ANSWER 10 OF 28 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1998:735041 CAPLUS

DOCUMENT NUMBER: 129:339871

TITLE: Hyaluronic acid and its salts inhibit

arterial restenosis

INVENTOR(S): Falk, Rudolf Edgar; Turley, Eva Anne;

Asculai, Samuel Simon

PATENT ASSIGNEE(S): Hyal Pharmaceutical Corporation, Can.

SOURCE: U.S., 15 pp., Cont.-in-part of U.S. Ser. No. 675,908.

CODEN: USXXAM

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 24

PATENT NO.	KIND DATE	APPLICATION NO.	DATE
US 5834444	A 19981110	US 1993-125398	19930923
CZ 288292	B6 20010516	CZ 1990-4598	19900921
US 6069135	A 20000530	US 1991-675908	19910703
US 5639738	A 19970617	US 1992-838675	19920221
US 5827834	A 19981027	US 1994-286263	19940805
US 6114314	A 20000905	US 1994-352697	19941201
US 5811410	A 19980922	US 1995-465335	19950605
US 5830882	A 19981103	US 1995-462615	19950605
US 5852002	A 19981222	US 1995-462147	19950605
US 5990095	A 19991123	US 1995-448503	19950726
US 6194392	B1 20010227		19950807
CA 2268476	AA 19980430		19961018
WO 9817320	A1 19980430		19961018
		BR, BY, CA, CH, CN, JP, KE, KG, KP, KR,	
		MW, MX, NO, NZ, PL,	, , , ,
		TT, UA, UG, US, UZ,	
KG. KZ. MD.		11, 0A, 0G, 03, 02,	VIV, API, AZ, DI,
		BE, CH, DE, DK, ES,	FT FR GR GR
		BF, BJ, CF, CG, CI,	
MR, NE, SN.		21, 20, 01, 00, 01,	0.1, 0.1, 0.1, 1.2,
AU 9672721	Al 19980515	AU 1996-72721	19961018
AU 739701	B2 20011018		
EP 952855	Al 19991103	EP 1996-934250	19961018
EP 952855	B1 20050727		
R: DE, FR, GB,	IT, SE		
NZ 335259	A 20001222	NZ 1996-335259	19961018
ZA 9608847	A 19970527	ZA 1996-8847	19961022
US 6475795	B1 20021105	US 1997-860696	19970616
US 2002077314	A1 20020620	US 1997-996470	19971222
US 6852708	B2 20050208		
US 2003036525	A1 20030220	US 2002-234355	20020904
PRIORITY APPLN. INFO.:		US 1991-675908	A2 19910703
		US 1992-838674	B2 19920221
		US 1992-838675	A2 19920221
		US 1992-952095	B2 19920928
•		CA 1989-612307	A 19890921
		WO 1990-CA306	W 19900918
		CS 1990-4598	A 19900921
		CA 1992-2061566	A 19920220
		US 1993-125398	A2 19930923 W 19940325
		WO 1994-CA188 US 1995-448503	W 19940325 Al 19950726
		03 1995-446503	WT T3320150

WO 1996-CA700 A 19961018 US 1997-860696 Al 19970616

AB A method is provided of preventing arterial restenosis of an animal after the arteries have been traumatized. The method comprises the administration of a therapeutically effective non-toxic amount of hyaluronic acid and/or pharmaceutically acceptable salts thereof to the animal to prevent narrowing of the arteries. The form of hyaluronic acid is selected from hyaluronic acid and pharmaceutically acceptable salts thereof having a mol. weight less than 750,000 daltons. **Hyaluronan** treatment of rabbits just prior to their injury abolished adherence of white cells to endothelium resulting in tissue that appeared intact as detected by hitol. criteria. REFERENCE COUNT: THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS 10 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 11 OF 28 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1998:653540 CAPLUS

DOCUMENT NUMBER: 129:255000

TITLE: Clearing of atherosclerosis with pharmaceutical

composition containing a chelating agent, a nonsteroidal antiinflammatory drug, an

antioxidant, and hyaluronic acid or a hyaluronic acid salt or derivative Falk, Rudolf Edgar; Asculai, Samuel Simon

INVENTOR(S): PATENT ASSIGNEE(S): Hyal Pharmaceutical Corporation, Can.

U.S., 5 pp., Cont.-in-part of U.S. Ser. No. 675,908. CODEN: USXXAM SOURCE:

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

		ENT				KIN		DATE			APPL	ICAT:	ION I	١٥.		D	ATE	
1 (	US CZ US	5817 2882 6069 2122	642 92 135			A B6 A AA		1998 2001 2000	0516 0530		US 1 CZ 1 US 1	990- 991-	4598 6759	08		1	9950 9900 9910	921 703
		5827						1995			CA 1 US 1	994-	2122	221			9940	
						A		1998			US 1	994-	2862	03			9940	
,	MO	9529 W:		70.00	וות	A1		1995			WO 1				DIC		9950	
		W :						BR, KE,										
								NZ,										
			TT,		MW,	MA,	NO,	NZ,	PL,	PI,	RO,	κυ,	Sυ,	SE,	56,	51,	SK,	TJ,
		DW.			GD.	67	шс	AT,	DF	CH	DE	Dν	P.C	ED	CD	CD	TO	TO
		1771.	TII	MC	NIT	от От	er,	BF,	DE,	CE,	CG,	CT,	CM	CV	CN.	ur,	TE,	II,
				TD.		Ε1,	36,	DE,	ы,	CE,	CG,	CI,	CM,	GA,	GIV,	MIL,	MK,	NE,
1	US 5811410							1998	0922		US 1	995-	4653	35		1	9950	605
	US 5830882							1998			US 1						9950	
	US 5852002							1 9 9 8	1222		119 1	995-	4621	47		1	9950	
	US 6194392							2001	0227		US 1	995-	4609	7.8		ī	9950	
								1998			CA 1						9961	
	CA 2268476 WO 9817320							1998			WO 1						9961	
		W:		AM.	AT.	A1		BB,							C7.			
			ES.	FI.	GB.	GE.	HU.	IL,	TS.	JP.	KE.	KG.	KP.	KR.	K7.	LK.	LR.	LS.
								MK,										
								TM,										
				KZ,					,	,	J,	,	υ,	02,	****	,	,	21,
		RW:						UG,	AT.	BE.	CH.	DE.	DK.	ES.	FT.	FR.	GB.	GR.
								PT,										
				NE,				•		,	,	,	,	,	,	<b>,</b>	,	,
i	AU	9672				A1		1998	0515		AU 1	996-	7272	1		1	9961	018
	ΑU	7397	01			B2		2001								_		
1	EΡ	9528	55			A1		1999	1103		EP 1	996-	9342	50		1	9961	018
1	EΡ	9528	55			В1		2005	0727									
		R:	DE,	FR,	GB,	IT,	SE											
1	ΝZ	3352				A		2000	1222		NZ 1	996-	3352	59		1	9961	018
	NZ 335259 ZA 9608847							1997			ZA 1						9961	
1	US 6475795							2002	1105		US 1	997-	8606	96		1	9970	616
1	US 2003036525							2003	0220		US 2					2	0020	904
PRIOR	RIORITY APPLN. INFO.:										US 1			80	i	A2 1	9910	703
											CA 1						9940	
											WO 1						9950	
											CA 1	989-	6123	07			9890	
											WO 1	990-	CA30	6	1		9900	
											CA 1 WO 1 CS 1	990-	4598				9900	

WO 1996-CA700 A 19961018 US 1997-860696 Al 19970616

A method of clearing atherosclerosis comprises administering to a patient at least one dosage amount of a pharmaceutical composition comprising an effective nontoxic amount of each of a chelating agent, a nonsteroidal antiinflammatory drug (NSAID), an

anti-oxidant and a form of hyaluronic acid,

selected from hyaluronic acid, salts thereof, homologs, analogs,

derivs., esters, complexes, fragments and subunits.

REFERENCE COUNT: THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 12 OF 28 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

1997:740122 CAPLUS

DOCUMENT NUMBER: TITLE:

128:7341 Use of forms of  $\ensuremath{\text{hyaluronic}}$  acid for the

treatment of cancer Falk, Rudolf Edgar

INVENTOR(S): PATENT ASSIGNEE(S):

Hyal Pharmaceutical Corporation, Can.; Falk, Rudolf

Edgar

SOURCE:

PCT Int. Appl., 35 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

1	PAT	ENT I	NO.			KIN	D	DATE			APPI	LICAT	ION I	NO.		D	ATE	
,	NO	9740	841			A1		1997	1106	,	WO 1	L997-	CA28	3		1	9970	428
		W:	AL,	AM,	AT,	ΑU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	CA,	CH,	CN,	CU,	CZ,	DE,
			DK,	EE,	ES,	FI,	GB,	GE,	ΗU,	IL,	IS,	JP,	ΚE,	KG,	ΚP,	KR,	ΚZ,	LC,
	LK, LR RO, RU AM, AZ			LR,	LS,	LT,	LU,	LV,	MD,	MG,	MK,	, MN,	MW,	MX,	NO,	NZ,	PL,	PT,
	RO, RU,			RU,	SD,	SE,	SG,	SI,	sĸ,	ТJ,	TM,	TR,	TT,	UA,	UG,	US,	UZ,	VN,
	AM, AZ,			ΑZ,	BY,	KG,	ΚZ,	MD,	RU,	TJ,	TM							
	AM, AZ, RW: GH, KE,		LS,	MW,	SD,	SZ,	UG,	ΑT,	BE,	CH,	DE,	DK,	ES,	FI,	FR,	GB,		
			GR,	ΙE,	IT,	LU,	MC,	NL,	PT,	SE,	BF,	BJ,	CF,	CG,	CI,	CM,	GΑ,	GN,
			ML,	MR,	NE,	SN,	TD,	TG										
(	CA	2175	282			AA		1997	1030		CA 1	L996-:	2175	282		1	9960	429
:	ZA 9703622				Α		1997	1125		ZA 1	L997-	3622			1	9970	425	
1	AU 9725644					A1		1997	1119		AU 1	L997-:	2564	4		1	9970	428
PRIOR:	IORITY APPLN. INFO.:				.:						CA 1	L996-:	2175	282	1	A 1	9960	429
	RO, F AM, A RW: GH, K GR, I ML, M CA 2175282 ZA 9703622 AU 9725644									1	WO 1	1997-6	CA28	3		<b>v</b> 7 1	9970	428

A method is provided for the treatment of **cancer** comprising AB administering orally or systemically (i.v. preferably) of an effective dosage amount of a form of hyaluronic acid selected from the group consisting of hyaluronic acid and pharmaceutically acceptable salts thereof as the only therapeutic agent, in a diluent, in such amts. and over such period of time to permit the successful treatment of cancer. Clin results are given.

L15 ANSWER 13 OF 28 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

1997:436579 CAPLUS

DOCUMENT NUMBER:

TITLE:

127:99842

Treatment of basal cell carcinoma and actinic

keratosis employing  ${\color{blue} \mathbf{hyaluronic}}$  acid and

NSAIDs

INVENTOR(S):

Falk, Rudolf Edgar; Asculai, Samuel Simon

PATENT ASSIGNEE(S):

Hyal Pharmaceutical Corp., Can.

SOURCE:

U.S., 19 pp., Cont.-in-part of U.S. Ser. No. 675,908.

CODEN: USXXAM Patent

DOCUMENT TYPE:

English

LANGUAGE:

FAMILY ACC. NUM. COUNT:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5639738	Α	19970617	US 1992-838675	19920221
CZ 288292	В6	20010516	CZ 1990-4598	19900921
US 6069135	A	20000530	US 1991-675908	19910703
CA 2061566	AA	19930821	CA 1992-2061566	19920220
CA 2061566	С	20020709		
US 5792753	A	19980811	US 1993-18508	19930217
US 6103704	Α	20000815	US 1993-18754	19930217
WO 9407505	A1	19940414	WO 1993-CA388	19930922

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AT, AU, BB, BG, BR, BY, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP,
             KP, KR, KZ, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD,
             SE, SK, UA, US, VN
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506 A 19970325 US 1994-285764
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PRIORITY APPLN. INFO.:
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                                              US 1997-860696
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                                                                    A3 19971020
    A method of treating a mammal for a condition of the skin or exposed
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AB A method of treating a mammal for a condition of the skin or exposed tissue selected from the group consisting of basal cell carcinoma and actinic keratosis is provided. The method consists essentially of topically administering to the site of the condition, more than once per day over a period of days sufficient to treat the condition, a non-toxic

effective dosage amount of a composition consisting essentially of (a) a non-steroidal anti-inflammatory drug (NSAID) in an amount sufficient to block prostaglandin synthesis, (b) hyaluronic acid or a pharmaceutically acceptable salt thereof in an amount effective to transport said NSAID into the skin or exposed tissue at the site of the condition. The concentration of the hyaluronic add or salt thereof is between 1-3% by weight of the composition The mol. weight of the hyaluronic acid or salt thereof is between 150,000 and 750,000 Daltons. A pharmaceutical excipient suitable for topical application is included. The NSAID in the composition may be diclofenac sodium.

L15 ANSWER 14 OF 28 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1997:289979 CAPLUS

DOCUMENT NUMBER: 126:259170

TITLE: Treatment of mucous membrane disease, trauma or

condition and for the relief of pain

INVENTOR(S): Asculai, Samuel Simon; Falk, Rudolf Edgar;

Russell, Alan L.

PATENT ASSIGNEE(S): Hyal Pharmaceutical Corporation, Can.

SOURCE: Can. Pat. Appl., 45 pp.

CODEN: CPXXEB

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PAT	CENT I	NO.			KIN	)	DATE					ION			D.	ATE	
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WO	9703	699			A1		1997	0206	1	WO 1	996-	CA48	8		1	9960	718
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IIA	9663		-				-	-				•				aasn	718
	7192									110 1	,,,	0331	,		_	,,,,,	,10
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	8390									EP 1	996-	9227	22		1	9960	718
EP	8390	52			Bl		2002	0508									
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		IE,	FI											-	-	•	•
JP	1151	4967			Т2		1999	1221		JP 1	996-	5061	20		1	9960	718
NZ	3120	73			А		2000	0228	1	NZ 1	996-	3120	73		1	9960	718
АТ	2171	97					2002						_				
	2176				T3		2002								_	9960	
	6159						2000									9971:	
PRIORITY			TNEO		^		2000	1212								9950	
ENTORIT	I APP.	TIA.	TMLO	• •										_	_		
										WO 1	996 <b>-</b>	CA48	8	1	w 1	9960	/T8

AB The use of an effective amount of a composition comprising an N.S.A.I.D. and a form of hyaluronic acid selected from hyaluronic acid, pharmaceutically acceptable salts thereof, fragments thereof and/or subunits thereof for mucous membrane trauma, disease, and/or pain relief. Clin. data are given for compns. containing hyaluronic acid and diclofenac Na.

L15 ANSWER 15 OF 28 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1996:153570 CAPLUS

DOCUMENT NUMBER: 124:194320

TITLE: Non-steroidal anti-inflammatory

agents and hyaluronic acid derivatives for

inhibition, control and regression of angiogenesis Willoughby, Derek A.; Alam, Chandan; Asculai, Samuel

S.; Falk, Rudolf E.; Harper, David W.

PATENT ASSIGNEE(S): Norpharmco Inc., Can. SOURCE: Can. Pat. Appl., 53 pp.

CODEN: CPXXEB

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

INVENTOR(S):

PATENT NO. KIND DATE APPLICATION NO. DATE

CA 2121454 AA 19951016 CA 1994-2121454 19940415
PRIORITY APPLN. INFO.: CA 1994-2121454 19940415

AB Non-steroidal anti-inflammatory agents, and

hyaluronic acid (I) and/or salts thereof and/or homologs, analogs, derivs., complexes, esters, fragments, and subunits of I, are used for the manufacture of a pharmaceutical composition for inhibition, controlling and/or regressing angiogenesis. Topical application of of 1% sodium hyaluronate and 6 mg/kg diclofenac acted synergistically and inhibited angiogenesis in rats.

L15 ANSWER 16 OF 28 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1996:145026 CAPLUS

DOCUMENT NUMBER: 124:165261

TITLE: Use of hyaluronic acid and forms to prevent

arterial restenosis

INVENTOR(S): Falk, Rudolf E.; Asculai, Samuel S.; Turley,

Eva A.

PATENT ASSIGNEE(S): Norpharmco Inc., Can. SOURCE: Can. Pat. Appl., 86 pp.

CODEN: CPXXEB

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CA 2120045	AA	19950926	CA 1994-2120045	19940325
CA 2120045	C	20000530		
PRIORITY APPLN. INFO.:			CA 1994-2120045	19940325
AB For the prevention	of the	narrowing o	f the tubular walls of	an animal
after the tubular	walls ha	ave been tra	umatized, the administ	ration of a
therapeutically ef	fective	non-toxic a	mount of <b>hyaluronic</b> act	id
and/or salts and/o	r homolo	ogs, analogs	, derivs., complexes, e	esters,
fragments, and sub-	units of	f hyaluronic	acid to the animal to	

L15 ANSWER 17 OF 28 CAPLUS COPYRIGHT 2005 ACS on STN

prevent narrowing of the tubular walls.

ACCESSION NUMBER: 1996:99453 CAPLUS

DOCUMENT NUMBER: 124:127136

TITLE: Pharmaceutical composition comprising

hyaluronic acid for the clearing of

arteriosclerosis

INVENTOR(S): Falk, Rudolf Edgar; Asculai, Samuel Simon

PATENT ASSIGNEE(S): Norpharmco Inc., Can. SOURCE: PCT Int. Appl., 21 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 24

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US	5827	834			Α		1998	1027		US 1	1994-	2862	63		1	9940	805	
ΑU	9523	800			A1		1995	1129		AU 1	1995-	2300	8		1	9950	427	
EΡ	7582	46			A1		1997	0219		EP 1	995-	9165	33		1	9950	427	
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US	5811	410			Α		1998	0922		US 1	995-	4653	35		1	9950	605	
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US	5852	002			Α		1998	1222		US 1	1995-	4621	47		1	9950	605	
US	6194	392			Bl		2001	0227		US 1	1995-	4609	78		1	9950	807	
US	5817	642			Α		1998	1006		US 1	1995-	4647	69		1	9950	815	
CA	2268	476			AA		1998	0430		CA 1	1996-	2268	476		1	9961	018	

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    A method of clearing atherosclerosis comprising the step of administering
     to a patient, at least one dosage amount of a pharmaceutical composition
     comprising an effective non-toxic amount of each of a chelating agent, a
     non-steroidal anti-inflammatory drug (NSAID),
     an anti-oxidant and a form of hyaluronic
     acid, selected from hyaluronic acid, salts thereof, homologs,
     analogs, derivs., esters, complexes, fragments and subunits. An i.v.
     solution contained EDTA 3, sodium ascorbate 12.5 g, diclofenac 15 , and sodium {\bf hyaluronate} 50 mg. The efficacy of composition was in
     treatment of atherosclerotic patients was shown.
L15 ANSWER 18 OF 28 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:
                          1996:43012 CAPLUS
DOCUMENT NUMBER:
                           124:66655
TITLE:
                           Pharmaceutical compositions comprising anti-
                           cancer drugs and hyaluronic acid for
                           treatment of cancer and metastasis
                           prevention
INVENTOR(S):
                           Falk, Rudolf Edgar; Asculai, Samuel Simon
                           Norpharmco Inc., Can.
PATENT ASSIGNEE(S):
SOURCE:
                           PCT Int. Appl., 255 pp.
                           CODEN: PIXXD2
DOCUMENT TYPE:
                           Patent
LANGUAGE:
                           English
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
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              MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ,
              TT, UA
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AU 696373

EP 760667

HU 75868

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             SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY,
         KG, KZ, MD, RU, TJ, TM
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                                               WO 1996-CA700
                                                                    A 19961018
                                               US 1997-860696
                                                                    A1 19970616
    A new method for the treatment of cancer in a human particularly
     malignant tumors, for example those in a breast or breasts, comprising the
     steps of: (1) directly injecting into the tumor a dosage amount of a
     pharmaceutical composition comprising an effective amount of an anti-
     cancer drug and/or drug suitable for use to treat cancer
     , such as mitoxantrone, and an effective amount of a form of
     hyaluronic acid or pharmaceutically acceptable salts thereof, such as sodium hyaluronate having a mol. weight of less than 750,000
     daltons, sterile water; and (2) administering systemically, preferably
     i.v., a dosage amount of a pharmaceutical composition comprising: (a) an
     effective amount of a form of hyaluronic acid or pharmaceutically
     acceptable salts thereof; (b) a drug selected from the group comprising: a non-steroidal anti-inflammatory drug, an anti-
     cancer drug, and a drug suitable for use to treat cancer
     and combination thereof optionally together with an antioxidant
     such as vitamin C. A patient with breast cancer was
     treated with non-steroidal anti-inflammatory drugs,
     sodium ascorbate hyaluronic acid i.v. The patient was also
     injected with mitoxantrone/hyaluronic acid on 4 occasions.
     Completed response with total regression of local tumor was observed and
     patient did not develop any metastases. Schedules for patients dosages
     are given.
L15 ANSWER 19 OF 28 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:
                          1995:967290 CAPLUS
DOCUMENT NUMBER:
                           124:789
TITLE:
                           Use of hyaluronic acid and forms thereof to
                           prevent arterial restenosis
INVENTOR(S):
                           Falk, Rudolf Edgar; Asculai, Samuel Simon;
                           Turley, Eva Anne
PATENT ASSIGNEE(S):
                           Norpharmco Inc., Can.
SOURCE:
                           PCT Int. Appl., 89 pp.
                           CODEN: PIXXD2
DOCUMENT TYPE:
                           Patent
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PATENT NO.
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WO 9526193
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                             19951005
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                                                                    19940325
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         PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, US, US, US, UZ, VN
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English

24

LANGUAGE:

FAMILY ACC. NUM. COUNT:

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RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE,
             BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG
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                                             US 1995-448503
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             SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY,
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             MR, NE, SN, TD, TG
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                           В1
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PRIORITY APPLN. INFO.:
                                                                  A2 19910703
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                                                                  A2 19920221
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                                                                  A 19890921
                                              WO 1990-CA306
                                                                  W 19900918
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                                                                     19900921
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                                             WO 1994-CA188
                                                                  W 19940325
                                              WO 1996-CA700
                                                                  A 19961018
                                              US 1997-860696
                                                                  A1 19970616
     For the prevention of the narrowing of the tubular walls of an animal
     after the tubular walls have been traumatized, a therapeutically effective
     nontoxic amount of hyaluronic acid, and/or a salt, homolog,
     analog, derivative, complex, ester, fragment, or subunit thereof, is
     administered to the animal to prevent narrowing of the tubular walls, e.g.
     arterial walls subjected to balloon angioplasty.
L15 ANSWER 20 OF 28 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:
                          1995:705578 CAPLUS
DOCUMENT NUMBER:
                          123:93340
TITLE:
                          Hyaluronic acid and forms to prevent
                          arterial restenosis
INVENTOR(S):
                          Falk, Rudolf E.; Asculai, Samuel S.; Turley,
                          Eva A.
PATENT ASSIGNEE(S):
                          Norpharmco Inc., Can.
SOURCE:
                          Can. Pat. Appl., 42 pp.
                          CODEN: CPXXEB
DOCUMENT TYPE:
                          Patent
LANGUAGE:
                          English
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
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PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CA 2106695	AA	19950323	CA 1993-2106695	19930922
CA 2106695	С	20000118		
PRIORITY APPLN. INFO.:			CA 1993-2106695	19930922
AB A method for prev	enting ar	rterial rest	enosis after trauma (e	g during
			dministration of a the dic acid and/or its sale	

and/or homologs, analogs, derivs., complexes, esters, fragments, and

subunits of hyaluronic acid and an agent selected from a

APPLICATION NO.

DATE

non-steroidal anti-inflammatory drug, restenosis
inhibiting drug, vitamin C, antioxidant, and free
radical scavenger.

L15 ANSWER 21 OF 28 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1995:524394 CAPLUS

DOCUMENT NUMBER: 122:256405

TITLE: Prevention and control of **cancer** with antiinflammatory agents and **hyaluronic** acid

DATE

INVENTOR(S): Falk, Rudolf E.; Asculai, Samuel S.

KIND

PATENT ASSIGNEE(S): Norpharmco Inc., Can. SOURCE: Can. Pat. Appl., 213 pp.

CODEN: CPXXEB

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION: PATENT NO.

---------CA 2097892 AA 19941207 CA 1993-2097892 19930607 PRIORITY APPLN. INFO.: CA 1993-2097892 19930607 A method of conditioning the immune system in humans to resist the formation of ≥1 cancerous tissue types comprises administering a nontoxic dosage amount of a composition comprising pharmaceutical excipients, a nonsteroidal antiinflammatory agent, hyaluronic acid and/or salts or derivs. thereof, and optionally vitamin C. Thus, repeated topical application of a 2.5% Na hyaluronate gel containing 3% Na diclofenac to basal cell carcinomas of the skin resulted in

regression and disappearance of the lesions.

L15 ANSWER 22 OF 28 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

1995:316085 CAPLUS

DOCUMENT NUMBER:

122:89434

TITLE:

Formulations containing  ${\color{blue} \mathbf{hyaluronic}}$  acid for

facilitation of drug transport

INVENTOR(S):

SOURCE:

Falk, Rudolf E.; Asculai, Samuel S.; Klein,

Ehud S.; Harper, David W.; Hochman, David; Purschke,

Don

PATENT ASSIGNEE(S):

Norpharmco Inc., Can. Can. Pat. Appl., 117 pp.

CODEN: CPXXEB

DOCUMENT TYPE:

Patent

LANGUAGE: English FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO. DATE KIND APPLICATION NO. DATE \_\_\_\_ ---------------CA 1993-2089621 CA 2089621 AΑ 19940817 PRIORITY APPLN. INFO.: CA 1993-2089621 19930216 Pharmaceutical compns. are provided from which effective nontoxic (to the patient) dosage amts. may be taken and applied to the skin and/or exposed tissue of a human, each effective dosage amount comprising pharmaceutical excipients suitable for topical application, an effective nontoxic dosage

exposed tissue, and an effective nontoxic dosage amount of hyaluronic acid or its salts, homologs, analogs, derivs.,

hyaluronic acid or its salts, homologs, analogs, derivs., complexes, esters, fragments, and/or subunits sufficient to facilitate or cause transport of the drug to a site in the skin, including epidermis or exposed tissue, resulting in its accumulation for a prolonged period of time. Thus, a gel containing glycerin 150, PhCH2OH 90, diclofenac Na 90, Na hyaluronate 75 g, and water 2795 mL, applied topically to

amount of a drug to treat a disease and/or condition of the skin and/or

cutaneous basal cell carcinoma several times a day for several wk, caused

disappearance of the carcinoma.

L15 ANSWER 23 OF 28 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

1995:309098 CAPLUS

DOCUMENT NUMBER:

122:64428

TITLE: Tre

Treatment of disease employing hyaluronic acid to facilitate transport of nonsteroidal

antiinflammatory drugs (NSAIDs)

INVENTOR(S):

Falk, Rudolf E.; Asculai, Samuel S.

PATENT ASSIGNEE(S):

Norpharmco Inc., Can. Can. Pat. Appl., 116 pp.

SOURCE:

CODEN: CPXXEB

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

AB A pharmaceutical composition comprises a plurality of effective nontoxic dosage amts. of a NSAID for topical administration to the site of pathol. and/or trauma of skin and/or exposed tissue of a human patient, combined with an effective nontoxic dosage amount of hyaluronic acid and/or its salts, homologs, analogs, derivs., complexes, esters, fragments, and/or subunits to facilitate or cause transport of the drug to the site of the pathol. and/or trauma. Thus, application of a formulation containing glycerin 150, PhCH2OH 90, diclofenac Na 90, Na hyaluronate 75 g, and water 2795 mL to an actinic keratosis lesion 3 times daily for 7 days resulted in complete resolution of the lesion.

L15 ANSWER 24 OF 28 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1995:275006 CAPLUS

DOCUMENT NUMBER: 122:38842

TITLE: Compositions for inhibition control and regression of

angiogenesis containing hyaluronic acid and

NSAID

INVENTOR(S): Willoughby, Derek A.; Alam, Chandan; Asculai, Samuel

Simon; Falk, Rudolf Edgar; Harper, David

William

PATENT ASSIGNEE(S): Norpharmco Inc., Can. SOURCE: PCT Int. Appl., 45 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PA'	rent	NO.			KIN		DATE				ICAT				I	DATE		
WO	9423				A1		1994	1027		WO 1	994-	CA20	7					
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		PL,	PT,	RO,	RU,	SD,	SE,	SI,	SK,	ТJ,	TT,	UΑ,	US,	UΖ,	VΝ			
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IL	1092 9465			A1		1999	0126		IL 1	994-	1092	93		1	.9940	411		
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ZA	9402	597			Α		1995	0208		ZA 1	994-	2597			1	9940	415	
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EP	6951	.87			A1		1996	0207		EP 1	994-	9134	64		1	.9940	415	
EP	6951	.87			Bl		2002	1030										
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JP	0850	8505			Т2		1996	0910		JP 1	994-	5225	74		1	9940	415	
HU	7446 2268	2			A2		1996	1230		HU 1	995-	113			1	9940	415	
AT	2268	27			E		2002	1115		AT 1	994-	9134	64		1	9940	415	
CN	1123	005			Α		1996	0522		CN 1	994-	1920	96		1	9940	515	
US	5847	002			Α		1998	1208		US 1	995-	4611	23		1	9950	605	
ИО	9504	073			Α		1995	1204		NO 1	995-	4073				9951	013	
FI	9504	914			Α		1995	1106		FI 1	995-	4914				9951	016	
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PRIORIT	Y APP	LN.	INFO	.:						CA 1	993-	2094	203		A :	9930	416	
										WO 1	994-	CA20	7		W :	9940	415	
										US 1	995-	4485	04		A3 :	9950	605	

AB The use of: (a) a non-steroidal anti-inflammatory agent, and (b) hyaluronic acid and/or salts thereof and/or homologous, analogs, derivs., complexes, esters, fragments, and subunits of hyaluronic acid, in the manufacture of pharmaceutical composition of inhibiting, controlling and/or regressing angiogenesis in a therapy wherein dosage amts. taken form the composition each comprise: (1) a therapeutically effective amount of component (a); and (2) a therapeutically effective amount of the hyaluronic acid and/or salts there of and/or homologous, analogs, derivs., complexes, esters, fragments, and sub-units of hyaluronic acid, the pharmaceutical composition being characterized in that for each dose amount taken from the pharmaceutical

composition, the amount of components (a) and (b) inhibit, control and/or regress angiogenesis.

L15 ANSWER 25 OF 28 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1994:315827 CAPLUS

DOCUMENT NUMBER: 120:315827

TITLE: Use of hyaluronic acid and forms thereof to

prevent arterial restenosis

INVENTOR(S): Falk, Rudolf Edgar; Asculai, Samuel Simon;

Turley, Eva Anne

Norpharmco Inc., Can. PCT Int. Appl., 60 pp. CODEN: PIXXD2 PATENT ASSIGNEE(S): SOURCE:

DOCUMENT TYPE: Patent LANGUAGE: English 24

FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

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PAT	CENT I	NO.			KIN	-	DATE			APE	L1	CAT	ION !	NO.		D	ATE		
WO	9407	505			A1		1994	0414		WO	19	993-	CA38	B		1	9930	922	
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	5639 2079				A A		1997 1994					,,,	8386° 2079:	. •			9920: 9920		
	2079				ς ΛΛ		1998			CA	1.3	,,,,,	2013.	203		1	9920	923	
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	9307				Α		1999						7221			1	9930	922	
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	5827 6114				A		1998	_		US	1 2	994-	2862 3526	07			9940		
	9501				82 A1 T2 E A2 A A B A A A A A A A A A A A A A A A A A		2000 1995						3326 1122	91			9941. 9950		
	3094				R1		2001			NO	13	) <b>, , ,</b> ,	1122			_	9930	323	
	6022				A		2000			IIS	10	95-	4037	66		1	9950	324	
	5811				A		1998			US	10	95-	4037 4653 4626	35		ī	9950		
	5830				Α		1998			US	19	95-	4626	15		ī	9950		
	5852				Α		1998						4621				9950		
IN	1812	88			Α		1998	0502		IN	19	95-	CA66	9		1	9950	613	
IN	1812	89			A		1998	0502		IN	19	95-	CA67	0		1	9950	613	
IN	1823	76			Α		1999	0403		IN	19	95-	CA67	1		1	9950	613	
	6194				B1		2001	0227		US	19	95-	4609	78		1	9950	807	
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	7029				B2		1999												
	2268				AA		1998			CA	19	996-	2268	476		1	9961		
WO	9817		D14		Al		1998			WO	Т :	,,,,,	CAIO	U			9961		
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	WM.						PT,												
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AII	9672		141,	J.,	Al		1998	0515		AII	1 (	996-	7272	1		1	9961	018	
	7397				B2		2001			٠.٠٠	1.	,,,,,		-		1	J J U I	010	
	9528				Al		1999			EР	10	996-	9342	50		1	9961	018	
	9528				Bl		2005							- •		_		0	
	R:		FR.	GB.	IT,														
NZ	3352		,	- •	Α΄		2000	1222		NZ	19	996-	3352	59		1	9961	018	
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19970527
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PRIORITY APPLN. INFO.:
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                                            IN 1993-CA554
                                                                Al 19930922
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                                           WO 1996-CA700
                                                                A 19961018
                                           US 1997-860696
                                                                Al 19970616
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AB For the prevention of the narrowing of the tubular walls of an animal after the tubular walls have been traumatized, a therapeutically effective nontoxic amount of hyaluronic acid and/or salts thereof and/or homologs, analogs, derivs., complexes, esters, fragments, and subunits thereof is administered. Results are presented which demonstrate that profound changes in the expression of hyaluronic acid and the receptor for hyaluronic acid-mediated motility occur after in vivo vascular injury and that the receptor-hyaluronic acid interaction is required for inflammatory cell chemotaxis and smooth muscle cell migration in vitro.

L15 ANSWER 26 OF 28 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1993:641409 CAPLUS

DOCUMENT NUMBER:

119:241409

TITLE:

119:241409

Topical composition containing hyaluronic

acid and nonsteroidal inflammation

inhibitors for treatment of skin diseases. Falk, Rudolf Edgar; Asculai, Samuel Simon

INVENTOR(S):
PATENT ASSIGNEE(S):

Norpharmco Inc., Can. PCT Int. Appl., 105 pp.

SOURCE: PCT Int. Appl.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent English

LANGUAGE:

FAMILY ACC. NUM. COUNT: 24

PAT	ATENT NO.				KIN	D	DATE			APP	LIC	AT:	I NO	NO.		D	ATE		
WO	9316																		
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CA	2061 2061	566			С		2002	0709											
ΑU	9334	889			A1		1993	0913		AU	199	3-:	3488	9		1	9930:	216	
EΡ	6268	64			A1		1994	1207		EP 1993-903755				1	9930	216			
EΡ	6268	64			B1		2003	0702											
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JΡ	0750	7054			Т2		1995	0803		JΡ	199	3-5	5144	80		1	9930	216	
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ΑТ	2440	20			E		2003	0715		AΤ	199	3-9	9037	55		1	9930	216	
PT	6268	64			T		2003	1128		PT	199	3-9	9037	55		1	9930	216	
ES	2202 2905	311			Т3		2004	0401		ES	199	3-9	9037.	55		1	9930	216	
CZ	2905	34			В6		2002	0814		CZ	199	3-2	229			1	9930	218	
ZA	9301	174			Α		1993	0916		ZĄ	199	3	1174			1	9930	219	
CA	2268	476			AA		1998	0430											
ΑU	9672	721			A1		1998	0515		ΑU	199	6-	7272	1		1	9961	018	
ΑU	7397	01			B2		2001	1018											
EΡ	9528	55			A1		1999	1103		EΡ	199	6-9	9342	50		1	9961	018	
EΡ	9528	55			B1		2005	0727											
	R:	DE,	FR,	GB,	IT,	SE													
ΝZ	3352 9608 6475	59			Α		2000	1222		ΝZ	199	6-3	3352	59		1	9961	018	
ZΑ	9608	847			Α		1997	0527		ZΑ	199	6-1	8847			1	9961	022	
US	6475	795			B1		2002	1105		US	199	7-1	3606	96		1	9970	616	
ΑU	9742	732			A1		1998	0115		ΑU	199	7-	4273	2		1	9971	020	

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     HK 1005982
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     AU 768058
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     US 2003036525
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                                 20030220
                                             US 2002-234355
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PRIORITY APPLN. INFO.:
                                             CA 1992-2061566
                                             CA 1992-2061703
                                                                 A 19920220
                                                                 A 19930216
A 19961018
                                             WO 1993-CA62
                                             WO 1996-CA700
                                             US 1997-860696
                                                                 Al 19970616
                                             AU 1997-42732
                                                                 A3 19971020
AB
   Diseases of skin and exposed tissue are treated topically in humans with
     mixts. of hyaluronic acid and prostaglandin synthesis
     inhibitors, preferably nonsteroidal antiinflammatory agents. A
     formulation comprised Na hyaluronate 37.5, diclofenac Na 45,
     benzyl alc. 15, methoxypolyethylene glycol 300 g, and 1,200 mL water. The
     formulation was used for treatment of basal cell carcinoma.
L15 ANSWER 27 OF 28 CAPLUS COPYRIGHT 2005 ACS on STN
                         1993:617437 CAPLUS
ACCESSION NUMBER:
DOCUMENT NUMBER:
                          119:217437
TITLE:
                         Drugs containing hyaluronic acid for the
                         topical treatment of skin diseases.
INVENTOR(S):
                         Falk, Rudolf Edgar; Asculai, Samuel Simon;
                         Klein, Ehud Shmuel; Harper, David William; Hochman,
David; Purschke, Don
PATENT ASSIGNEE(S):
                         Norpharmco Inc., Can.
PCT Int. Appl., 106 pp.
SOURCE:
                         CODEN: PIXXD2
DOCUMENT TYPE:
                         Patent
LANGUAGE:
                         English
FAMILY ACC. NUM. COUNT:
                         24
PATENT INFORMATION:
                         KIND DATE
     PATENT NO.
                                             APPLICATION NO.
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WO	9316	732			Al 1993090			0902	1	พด	190	33-0	°A61			1 1	9930	216	
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		BF.	B.I.	CF.	CG,	CT	CM	GA,	GN,	MT.	, ,	AD,	SNI	TO,	TC,	ML,	ш,	36,	
CA	2061	703	Бо,	CL,	20,	C1,	1993	0A,	GIV,	~D	100	'IIV,	2061.	703	10	1.	9920	220	
CA	2061	703			~~		2002	0702		CA	101	JZ-1	2001	, 03		1	<i>3320.</i>	220	
AII	2061 2061 9334 6268 6268	888			Δ1		1993	0102		וומ	1 00	33-	3/88	2		1 .	9930	216	
EP	6268	63			Al		1994	1207		r D	1 9 0	33-	9037	5 5 <i>1</i>		1	9930	216	
EP	6268	63			B1		2001	0425			1).		,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	J4		1.	9930.	210	
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TN	1759	18			A		1995	1028		TNI	1 90	33_0	ים פער מים מים	•		1.	9930	216	
HII	7508	9			A2		1997	0428		HII	190	33-	3292			1	9930	216	
PT.	1732	11			R1		1998	0720		DT.	190	33_	3011	4 0		1	9930. 9930	216	
NZ.	2992	80			A		2000	1222		NZ	190	33-	2992	80		1	9930.	216	
AT	2007	36			F		2000	0515		አጥ	100	33-6	とフラム・	5.4		1.	2230.	216	
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PT	6268	63			T		2001	0830		ᅋ	190	33-	2037.	54		1	9930.	216	
CZ	2906	37			B6		2001	0030		C7	100	33-	230 230	J4		1	9930	210	
CN	1084	064			A		1994	0323		CNI	190	33-	10341	9.9		1 .	9930	220	
CN	1103	219			B		2003	0319		···			1034			1	,,,,,,,	220	
FT	9403	789			Δ		1994	1003		FT	1 0 0	4-1	3789			1 .	9940	917	
FT	1135	22			R1		2004	0514			1).		3,03			1	J J 4 U	017	
NO	9403	044			A		1994	1019		NΩ	190	94 – 1	3044			1 .	9940	817	
NO	3129	39			B1		2002	0722					3011			-	,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	01,	
TN	1791	30			A		1997	กรรถ		TN	1 90	95-0	7227	2		1 .	9950	313	
IN	1822	67			A		1999	0227		TN	190	95-0	CA27	n		1	995N	313	
IN	1823	48			A		1999	0327		TN	190	95-0	A27	1		1	9950	313	
IN	1782	80			A		1997	0322		TN	199	95-0	7A29	3		1	9950	314	
US	6140	312			Δ		2000	1031		IIS	190	95-	1667	1 4		1 1	9950	606	
CA	2268	476			44		1998	0430		C 2	190	96-	2268	176		1 4	9961	018	
All	9672	721			A1		1998	0515		וומ	190	96-	7272	1		1 .	9961	018	
AII	7397	01			B2		2001	1018	•	110		, ,		-		-	J J O I .	010	
EP	7397 9528 9528	55			Al		1999			FP	1 90	96-9	9342	50		1 .	9961	018	
EP	9528	55			RI		2005						JJ42.	30		1	J 5 G 1 1	010	
	R:	DF	FP	GB	IT,	C.F.		0,2,											
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7.A	9608	847			7		1997	1527		7 D	190	26-G	3332; 88 <i>4</i> 7	J		1 1	2201'	023	
US	6475	795			p1		2002	1105	,	116	100	37-9	960 <i>61</i>	٥٤		1.1	シフロエリ	044 616	
AII	3352 9608 6475 9742	732			<u>Δ</u> 1		1002	1103		וומ	100	27-	4272	20		1 1	221U	U3U 010	
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                         A1
                                           US 2002-234355
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PRIORITY APPLN. INFO.:
                                           CA 1992-2061703
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                                           CA 1992-2061566
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                                           IN 1993-CA94
                                                               Al 19930216
                                           WO 1993-CA61
                                                               A 19930216
                                           WO 1996-CA700
                                                               A 19961018
                                           US 1997-860696
                                                               Al 19970616
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AB Compns. comprising hyaluronic acid and a nonsteroidal antiinflammatory agent or a neoplasm inhibitor are topical drugs for the treatment of skin diseases, especially cancers. A formulation comprised diclofenac sodium 45, Na hyaluronate 37.5, benzyl alc. 15, methoxypolyethylene glycol 300 g, and water to 1200 mL. The formulation was successful in the treatment of human basal cell carcinoma. Hyaluronic acid facilitates transport of the 2nd drug.

L15 ANSWER 28 OF 28 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1992:51600 CAPLUS

DOCUMENT NUMBER: 116:51600

TITLE: Hyaluronic acid and derivatives for

facilitating penetration of therapeutic agents in

treatment of conditions and diseases Falk, Rudolf Edgar; Asculai, Samuel S.

INVENTOR(S): PATENT ASSIGNEE(S):

Norpharmco Inc., Can. PCT Int. Appl., 116 pp. SOURCE: CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 24

PAT	TENT NO.		KIN	D	DATE			API	PLI	CAT	ION	NO.		D.	ATE		
	9104058			A2		1991	0404		WO	19	90-	CA30	6		1	9900	918
MO	9104058			A3		1991	0919										
	W: AT,	ΑU,	BB,	BG,	BR,	CA,	CH,	DE,	DF	<, I	ES,	FI,	GB,	ΗU,	JP,	KP,	KR,
	LK,	LU,	MC,	MG,	MW,	NL,	NO,	RO,	SI	ο, :	SE,	SU,	US				
	RW: AT,	BE,	BF,	BJ,	CF,	CG,	CH,	CM,	DE	Ξ,	DK,	ES,	FR,	GΑ,	GB,	IT,	LU,
		MR,	NL,	SE,	SN,	TD,	TG										
	1340994			A1		2000 1991 1991	0516		CA	19	89-	6123	07		1	9890	921
	2042034			AA		1991	0322		CA	19	90-	2042	034		1	9900	918
	9064330			A1		1991	0418		ΑU	19	90-	6433	0		1	9900 9900 9900	918
	445255			A1		1991 1995	0911		ΕP	19	90-	9141	08		1	9900	918
EP	445255			B1		1995	1206										
EΡ	445255																
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BR	9006924			A		1991	1210		BR	19	90-	6924			1	9900	
JP	04504579			Т2		1992	0813		JP	19	90-	5132	04		1	9900	918
JP	3256761			B2		2002	0212										
HU	64699			A2		1994	0228		HU	19	90-	7339	H		1	9900	
EP	9006924 04504579 3256761 64699 656213 656213			A1		1995	0607		ΕP	19	95-	1001	86		1	9900	918
EΡ																	
	R: AT,	BE,	CH,	DE,	DK,									SE			
	131068			E T3		1995							80			9900	
	2080837			Т3			0216						08			9900	
	112812			B1 C1 E			0130		RO	19	90-	1485	11		1	9900	918
	2146139			C1		2000 2002	0310		RU	19	90-	4895	848 86		1	9900	918
	227587			E					AT	19	95-	1001	86		1	9900	918
	2186693			Т3			0516		ES	19	95-	1001	86		1	9900	918
	95745			A1 A			0922		IL	19	90-	9574	5 40		1	9900	919
							0522		CN	19	90-	1088	40		1	9900	921
	1101228			В		2003											
	9007564			A A		1991			ZA	19	90-	7564			1	9900 9900	921
	171745					1992							1		1	9900	921
	9101952			A		1991										9910	
	6069135			A		2000							08			9910	
	9352274					1994			ΑU	19	93-	5227	4		1	9931	209
	674894			В2		1997											
	3545			В		1995	—		LT	19	93-	1282			1	9931	
	5827834					1998			US	19	94-	2862	63		1	9940	
	5910489			A		1999			US	19	94-	2908	48		1	9940	
	5811410			• • •		1998							35			9950	
	5830882			A			1103						15				
	5852002 5914314			A		1998			US	19	95-	4621	47		1	9950	605
US	2914314			Α		1999	0622		US	19	95-	4626	14		1	9950	605

	5000040	70	19990727	110	1995-462148		10050605
	5929048	A					19950605
	5932560	A	19990803		1995-461124		19950605
	5985850	A	19991116		1995-462154		19950605
	6048844	A	20000411		1995-461565		19950605
	5962433	A	19991005		1995-466778		19950606
	6017900	Α	20000125		1995-466775		19950606
	6218373	B1	20010417		1995-467994		19950606
	6194392	B1	20010227		1995-460978		19950807
	2268476	AA	19980430	-	1996-2268476		19961018
AU	9672721	A1	19980515	AU	1996-72721		19961018
AU	739701	B2	20011018				
EP	952855	A1	19991103	EP	1996-934250		19961018
EP	952855	B1	20050727				
	R: DE, FR, GB,	IT, SE					
NZ	335259	A	20001222	NZ	1996-335259		19961018
ZA	9608847	A	19970527	ZA	1996-8847		19961022
US	5985851	Α	19991116	US	1996-744852		19961118
AU	9714850	A1	19970522	ΆU	1997-14850		19970221
US	6475795	Bl	20021105	US	1997-860696		19970616
HK	1005985	A1	20030214	HK	1998-105089		19980610
US	2003036525	A1	20030220	US	2002-234355		20020904
US	2004019011	A1	20040129	US	2003-628999		20030728
PRIORITY	Y APPLN. INFO.:			CA	1989-612307	Α	19890921
				EP	1990-914108	A3	19900918
				WO	1990-CA306	Α	19900918
				US	1991-675908	A1	19910703
			•	CA	1992-2061566	Α	19920220
				CA	1992-2061703	Α	19920220
				US	1992-838674	B2	19920221
				US	1992-838675	A2	19920221
				US	1994-290848	A3	19940819
				US	1994-290840	АЗ	19941027
				WO	1996-CA700	Α	19961018
				US	1997-860696	A1	19970616
				US	2000-547394	Bl	20000411
AD DU	aluronic acid i	a incli	iding ite	calte	homologues	2221000	

AB Byaluronic acid, i.e. including its salts, homologues, analogs, derivs., complexes, esters, or fragments of its subunits, is used in combination with therapeutic agents to facilitate the agent's penetration through the tissue or cell membrane to enhance the effectiveness and lower the dose and toxicity of the therapeutic agent, or to help to remove toxic substances from the target cell or tissue for treatment of diseases or conditions. The therapeutic agents are selected from a free radical scavenger, ascorbic acid, an anti-cancer agent, chemotherapeutic agent, anti-viral agent, etc. The diseases or conditions include cancer, herpes, canker sore, psoriasis, mononucleosis, post-menopause, control of fertility, renal failure, cardiac insufficiency, hypertension, edema, transplants, AIDS, detoxification, etc. Clin. studies are presented.

MEDLINE on STN L22 ANSWER 1 OF 23 2002334400 ACCESSION NUMBER: MEDLINE DOCUMENT NUMBER: PubMed ID: 12077476

Discernment of adipose versus nervous tissue: a novel TITLE:

adjunct solution in lipomyelomeningocele surgery.

AUTHOR: Patwardhan Ravish V; Tubbs R Shane; Leonard Robert J; Kelly David; Killingsworth Cheryl R; Rollins Dennis L; Smith

William M; Ideker Raymond E; Oakes W Jerry

CORPORATE SOURCE: Division of Neurosurgery, The Children's Hospital of

Alabama, Birmingham, AL, USA.. rpatwardhan@sport.rr.com

Pediatric neurosurgery, (2002 Jun) 36 (6) 314-9. Journal code: 9114967. ISSN: 1016-2291.

PUB. COUNTRY: Switzerland

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

SOURCE:

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200209

Entered STN: 20020623 ENTRY DATE:

Last Updated on STN: 20020911 Entered Medline: 20020910

OBJECTIVE: To determine a solution capable of discerning adipose versus nervous tissue, to aid in surgical separation of the adipose tissue which appears to be visually indistinguishable from nervous tissue in lipomyelomeningoceles (LMMs). METHODS: The following solutes (in normal saline) were investigated, both at 25 and 37 degrees C: beta-carotene, vitamin D, vitamin E, lecithin, hydrogen peroxide, lipase, protease, hyaluronidase, partially purified collagenase, purified collagenase, trypsin, trypsin plus purified collagenase and non-solute-containing saline (control). Each solution was applied to a pediatric lipoma to determine gross effects over a period of approximately 30 min. If a solution appeared to affect the adipose tissue grossly, studies of functional in vivo sensory evoked and spontaneous potentials using that particular solution were conducted upon sheep spinal cord, nerve roots, dura and peripheral nerve. Additionally, histological studies were conducted to determine the effect of that solution upon adipose tissue, spinal cord, myelin, dura and nerve roots. RESULTS: Of all solutions investigated, partially purified collagenase type 1 (T1C; Lot MOM4322, Code CLS-1, Worthington Biochemical Corporation, Lakewood, N.J., USA) at 37 degrees C was the most successful in grossly altering the consistency and appearance of adipose tissue. This change was more apparent over 20-30 min following application of the solution to the adipose tissue. Solutions not containing TlC did not show appreciable results; purified collagenase plus trypsin did not appear comparable or superior to TlC. No significant histological or functional change was noted when comparing the spinal cord, nerve rootlets, myelin, dura or peripheral nerve from the T1C-treated group versus normal (untreated) control groups. CONCLUSION: TiC appears to be a potentially effective solution for application during LMM surgery in the acute setting, and such use of an adjunct solution may significantly aid in the safe surgical resection of LMMs. Pending further research, this technique may be applied for other indications which require discernment or alteration of adipose versus nervous tissue. Copyright 2002 S. Karger AG, Basel

L22 ANSWER 2 OF 23 MEDLINE on STN ACCESSION NUMBER: 1998331852 MEDLINE

Ascorbic acid in the prevention and treatment of cancer.

AUTHOR: Head K A

DOCUMENT NUMBER:

CORPORATE SOURCE: Alternative Medicine Review. P.O. Box 25, Dover, ID 83825,

USA.. kathi@thorne.com

PubMed ID: 9630735

SOURCE: Alternative medicine review : a journal of clinical therapeutic, (1998 Jun) 3 (3) 174-86. Ref: 63

Journal code: 9705340. ISSN: 1089-5159.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

General Review; (REVIEW)

LANGUAGE: English

FILE SEGMENT: Consumer Health

ENTRY MONTH: 199807

ENTRY DATE: Entered STN: 19980811

> Last Updated on STN: 19980811 Entered Medline: 19980728

AΒ Proposed mechanisms of action for ascorbic acid (ascorbate. vitamin C) in the prevention and treatment of cancer include

enhancement of the immune system, stimulation of collagen formation necessary for "walling off" tumors, inhibition of hyaluronidase which keeps the ground substance around the tumor intact and prevents metastasis, prevention of oncogenic viruses, correction of an ascorbate deficiency often seen in cancer patients, expedition of wound healing after cancer surgery, enhancement of the effect of certain chemotherapy drugs, reduction of the toxicity of other chemotherapeutic agents such as Adriamycin, prevention of free radical damage, and neutralization of carcinogenic substances. as well as Japanese studies have pointed to the potential benefit of high dose vitamin C for the treatment of "terminal" cancer. Mayo Clinic studies, however, have contradicted the Scottish and Japanese findings, resulting in accusations of methodological flaws from both sides. Numerous epidemiological studies have pointed to the importance of dietary and supplemental ascorbate in the prevention of various types of cancer including bladder, breast, cervical, colorectal, esophageal, lung, pancreatic, prostate, salivary gland, stomach, leukemia, and non-Hodgkin's lymphoma.

L22 ANSWER 3 OF 23 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2004:110793 BIOSIS DOCUMENT NUMBER: PREV200400112259

TITLE: Andrology lab corner: Nurture vs nature: How can we

optimize sperm quality?.

AUTHOR(S): Alvarez, Juan G. [Reprint Author]

CORPORATE SOURCE: Centro de Infertilidad Masculina, C/Fernando Macias, 8, 1C,

15004, La Coruna, Spain

jalvarez@androgen.es

SOURCE: Journal of Andrology, (September-October 2003) Vol. 24, No.

5, pp. 640-648. print.

ISSN: 0196-3635 (ISSN print).

DOCUMENT TYPE: Article LANGUAGE: English

ENTRY DATE: Entered STN: 25 Feb 2004

Last Updated on STN: 25 Feb 2004

L22 ANSWER 4 OF 23 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.

on STN

ACCESSION NUMBER: 2002189566 EMBASE

TITLE: Treatment options in extravasation injury: An experimental

study in rats.

AUTHOR: Yilmaz M.; Demirdover C.; Mola F.

CORPORATE SOURCE: Dr. C. Demirdover, Dokuz Eylul Univ. Tip Fakultesi, Plast.

Rekonstr. Cerrahi Anabilim, 35340 Inciralti, Izmir, Turkey.

 ${\tt cenkddr@mailcity.com}$ 

SOURCE: Plastic and Reconstructive Surgery, (2002) Vol. 109, No. 7,

pp. 2418-2423.

Refs: 17

ISSN: 0032-1052 CODEN: PRSUAS

COUNTRY: United States
DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 009 Surgery

013 Dermatology and Venereology

016 Cancer

037 Drug Literature Index

052 Toxicology

LANGUAGE: English SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 20020613

Last Updated on STN: 20020613

AB Local skin necrosis after extravasation of doxorubicin hydrochloride (Adriamycin), a widely used **chemotherapeutic** agent, is a common problem in cancer patients. Even though several treatment options have been proposed for extravasation injury, there is still controversy regarding the management of such lesions. The aim of this study was to compare the efficacy of saline infiltration, **vitamin** C infiltration, suction technique, and early surgical excision as a treatment in a rat extravasation model. The authors planned their study in two stages. In stage 1, the lowest effective dose of doxorubicin at which a homogeneous skin necrosis was formed and the method of administration were investigated. Intradermal and sub-pannicular injections were made for six rats, using six different concentrations of doxorubicin (0.33, 0.5, 0.66, 1.0, 1.33, and 1.5 mg/ml). In stage 1, the intradermal injection produced homogeneous and uniform tissue necrosis. In stage 2, the efficacy of saline infiltration (group 1), **vitamin** C infiltration (group 2), suction (group 3), suction and saline washout

(group 4), suction and vitamin C washout (group 5), and early surgical excision (group 6) was compared. The treatment options were applied 2 hours after doxorubicin injection. At the end of the seventh day, the presence and size of ulcers at the injection site were calculated. Fourteen days after injection, a histopathologic examination was performed for each treatment and control group. In groups 1 and 3, there was no statistically significant difference in the size of necrosis compared with the control groups. In groups 2, 4, and 5, the size of necrosis was smaller compared with the control groups, and this was statistically significant. Furthermore, in group 4 (suction and saline washout) and group 5 (suction and vitamin C washout), the calculated area of necrosis was smaller compared with other treatment groups, and this was statistically significant. The findings supported the assertion that suction and saline or vitamin C washout reduce necrotic tissue size in extravasation injury.

L22 ANSWER 5 OF 23 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.

on STN

ACCESSION NUMBER: 86082950 EMBASE

DOCUMENT NUMBER:

1986082950

TITLE:

[Extravasation after use of antitumors drugs: Clinical experiences, procedures of prevention and therapy]. LESIVITA CUTANEA DA ANTIBLASTICI. ESPERIENZA CLINICA,

MODALITA DI PREVENZIONE E TERAPIA.

AUTHOR: Villani C.; Doninelli M.; Giobbi L.; et al.

CORPORATE SOURCE:

II Clinica Ostetrica e Ginecologica dell'Universita La Sapienza di Roma, Insegnamento di Ginecologia Oncologica,

Roma, Italy

SOURCE:

Patologia e Clinica Ostetrica e Ginecologica, (1985) Vol.

13, No. 4, pp. 267-272.

CODEN: PCOGBW

COUNTRY:

Italy DOCUMENT TYPE: Journal

FILE SEGMENT:

038 Adverse Reactions Titles

037 Drug Literature Index 010 Obstetrics and Gynecology 013 Dermatology and Venereology

LANGUAGE: Italian

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 911210

Last Updated on STN: 911210

L22 ANSWER 6 OF 23 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.

on STN

ACCESSION NUMBER: 86009829 EMBASE

DOCUMENT NUMBER:

1986009829

TITLE:

[The treatment of local toxic reactions due to antitumour's

agents1.

IL TRATTAMENTO DELLE REAZIONI TOSSICHE LOCALI DA AGENTI

ANTINEOPLASTICI.

Pollera C.F.; Mazza D.; Nardi M.; et al.

CORPORATE SOURCE: Ispettorato di Sanita della Marina Militare, Roma, Italy

SOURCE: Annali di Medicina Navale, (1985) Vol. 90, No. 1, pp.

163-178. CODEN: AMDNA4

COUNTRY: Italv

DOCUMENT TYPE: Journal

FILE SEGMENT: 038 Adverse Reactions Titles 037 Drug Literature Index

LANGUAGE: **Italian** 

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 911210

Last Updated on STN: 911210

L22 ANSWER 7 OF 23 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.

on STN

ACCESSION NUMBER: 74128863 EMBASE

DOCUMENT NUMBER: 1974128863

TITLE: Changes in glycosaminoglycans of AH 130 ascites tumor after

treatment with cyclophosphamide and vitamin A. AUTHOR: Suematsu T.; Nakamura N.; Kamada T.; Abe H. CORPORATE SOURCE: Dept. Med., Osaka Univ. Med. Sch., Osaka, Japan

SOURCE: Cancer Research, (1973) Vol. 33, No. 11, pp. 2862-2866.

CODEN: CNREA8

DOCUMENT TYPE: Journal

FILE SEGMENT: 037 Drug Literature Index 016 Cancer

030 Pharmacology

029 Clinical Biochemistry

005 General Pathology and Pathological Anatomy

LANGUAGE: English

A large amount of glycosaminoglycans was found in the AH 130 ascites tumor cells and also in the ascites fluids. After combined administration of cyclophosphamide and vitamin A to the tumor bearing rats, a significant decrease was found in tumor glycosaminoglycans sensitive to lysosomal hyaluronidase, such as the nonsulfated glycosaminoglycans or chondroitin sulfate A and/or C. An increased release of the lysosomal enzymes into ascites was also consistently found. It is suggested that this reduction in tumor glycosaminoglycans reflects the synergistic effect of the combined administration of cyclophosphamide and vitamin A on the survival time of tumor bearing rats in this investigation.

L22 ANSWER 8 OF 23 CAPLUS COPYRIGHT 2005 ACS on STN

2005:611948 CAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER: 143:126813

TITLE: Treatment of ophthalmic conditions Osio Corp., USA; Osio Sancho, Alberto PATENT ASSIGNEE(S):

PCT Int. Appl., 51 pp. SOURCE:

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE --------------------20050714 WO 2004-US42660 A2 WO 2005062818 20041217 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: MX 2003-11987

A 20031219 Ophthalmic conditions such as presbyopia, myopia, and astigmatism can be corrected by the use of a molding contact lens in combination with a pharmaceutical composition suitable for delivery to the eye. The molding contact lenses are preferably com. available and are not specifically designed for orthokeratol. The agents in the pharmaceutical compns. such as hyaluronase allow the cornea of the eye to be molded in order to correct the refractive error of the eye. The contact lenses and the pharmaceutical composition induce a change in the radius of curvature of the anterior surface of the cornea, thereby correcting the refractive error of the eye. One advantage of the inventive technique is that the patient with his or her own individual visual needs guides the treatment until the patient near and far visual needs are met. The invention also provides for kits, which contain molding contact lenses, pharmaceutical composition suitable for delivery to the eye, and instructions, useful in the inventive system.

L22 ANSWER 9 OF 23 CAPLUS COPYRIGHT 2005 ACS on STN

2005:570378 CAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER: 143:103333

TITLE: Collagen matrix for soft tissue augmentation

INVENTOR(S): Freeman, Lynetta J.; Roweton, Susan; Walthall, Ben;

Nguyen, Kien T.

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 16 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

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10/628.999
     US 2005142161
                            A1
                                   20050630
                                                US 2003-748894
                                                                          20031230
     CA 2491788
                            AΑ
                                   20050630
                                                CA 2004-2491788
                                                                          20041224
                                               EP 2004-258168
                                                                          20041229
     EP 1555035
                            A2
                                   20050720
         R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, BA, HR, IS, YU
     JP 2005193055
                            A2
                                   20050721
                                                JP 2005-202
                                                                          20050104
                                                                      A 20031230
PRIORITY APPLN. INFO.:
                                                US 2003-748894
    The present invention includes methods and materials for soft tissue
     implant formed from biol.-compatible polymeric matrixes. The matrixes may
     have pores sized for in-growth of soft tissue. The material may be
     utilized with collagen or other matrix materials. This material may be
     used in a method of reforming soft tissues by implanting the material
     within soft body tissues to modify soft tissue defects such as wrinkles or
     biopsy tissue defects and to reshape soft tissue. An in vivo evaluation
     of the com.-available Integra Life Sciences scaffold (without the silicone backing) as a subdermal defect filler was performed. Sheets and rolls (2
     cm in length, 0.5 cm in diameter) of Integra were implanted subdermally over
     the ventral thoracic and abdominal regions of six pigs. Explant time
     periods for this study was 14, 42, and 180 days. The Integra material
     demonstrated acceptable biocompatibility in this study.
L22 ANSWER 10 OF 23 CAPLUS COPYRIGHT 2005 ACS on STN
                           2005:471831 CAPLUS
ACCESSION NUMBER:
DOCUMENT NUMBER:
                           143:1254
TITLE:
                           Combinations and methods for treating neoplasms
INVENTOR(S):
                           Yu, Baofa
PATENT ASSIGNEE(S):
                           USA
                           U.S. Pat. Appl. Publ., 34 pp., Cont.-in-part of U.S. Ser. No. 765,060.
SOURCE:
                           CODEN: USXXCO
DOCUMENT TYPE:
                           Patent
LANGUAGE:
                           English
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
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PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005118187	A1	20050602	US 2004-973798	20041025
US 2002044919	A1	20020418	US 2001-765060	20010117
US 6811788	B2	20041102		
PRIORITY APPLN. INFO.:			US 2000-177024P	P 20000119
			US 2001-765060	A2 20010117

AB Methods for treating neoplasms, tumors and cancers, using one or more haptens and coagulation agents or treatments, alone or in combination with other anti-neoplastic agents or treatments, are provided. Also provided are combinations, and kits containing the combinations for effecting the therapy.

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L22 ANSWER 11 OF 23 CAPLUS COPYRIGHT 2005 ACS on STN ACCESSION NUMBER: 2005:300435 CAPLUS
```

DOCUMENT NUMBER: 142:373859

TITLE: Preparation of pyrimidine and pyridine derivatives

useful as HMG-CoA reductase inhibitors

INVENTOR(S): Ahmad, Saleem; Robl, Jeffrey A.; Ngu, Khehyong

PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA

SOURCE: PCT Int. Appl., 103 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT NO.		KINI	) i	DATE		1				NO.		D/	ATE	
WO 20050307	58	A1	:	2005	0407	7	NO 2	004-1	JS31:	212		20	0040	922
W: AE,	AG, AL	, AM,	AT,	ΑU,	ΑZ,	BA,	BB,	BG,	BR,	BW,	BY,	BZ,	CA,	CH,
CN,	CO, CR	, CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	EG,	ES,	FI,	GB,	GD,
GE,	GH, GM	, HR,	ΗU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,	ΚP,	KR,	ΚZ,	LC,
LK,	LR, LS	, LT,	LU,	LV,	ΜA,	MD,	MG,	MK,	MN,	MW,	MX,	ΜZ,	NA,	NI,
NO,	NZ, OM	, PG,	PH,	PL,	PT,	RO,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	SY,
ТJ,	TM, TN	, TR,	TT,	ΤZ,	UA,	UG,	US,	UZ,	VC,	VN,	YU,	ZA,	ZM,	ZW
RW: BW,	GH, GM	, KE,	LS,	MW,	ΜZ,	NA,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AM,
AZ,	BY, KG	, KZ,	MD,	RU,	ТJ,	TM,	ΑT,	ΒE,	BG,	CH,	CY,	CZ,	DE,	DK,
EE,	ES, FI	, FR,	GB,	GR,	ΗU,	ΙE,	ΙT,	LU,	MC,	NL,	PL,	PT,	RO,	SE,
SI,	SK, TR	, BF,	ВJ,	CF,	CG,	CI,	CM,	GΑ,	GN,	GQ,	GW,	ML,	MR,	ΝE,

SN, TD, TG

US 2005085497 A1 20050421 US 2004-946055 20040921 PRIORITY APPLN. INFO.: US 2003-505893P P 20030925

MARPAT 142:373859 OTHER SOURCE(S):

Title compds. I [X = N, CR5; R1-2 = H, alkyl, alkoxyalkyl, etc.; R3 =(hetero)aryl, cycloalkyl, etc.; R4 = H, (cyclo)alkyl, haloalkyl, etc.; R5 = H, alkyl; Z = hydroxyalkyl, etc.] are prepared For instance, II is prepared in 5 steps from a substituted pyrimidine, 2-methyl-2H-[1,2,4]triazol-3ylamine, and a prior art homochiral dihydroxy acetonide derivative I are HMG-CoA reductase inhibitors and are active in inhibiting cholesterol biosynthesis, modulating blood serum lipids, for example, lowering LDL cholesterol and/or increasing HDL cholesterol, and treating hyperlipidemia, dyslipidemia, hormone replacement therapy, hypercholesterolemia, hypertriglyceridemia and atherosclerosis as well as

Alzheimer's disease and osteoporosis [no data].

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 12 OF 23 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:161960 CAPLUS

DOCUMENT NUMBER: 142:266701

TITLE: Megalin-based delivery of therapeutic compounds to the

brain and other tissues

INVENTOR(S): Zankel, Todd; Starr, Christopher M.

PATENT ASSIGNEE(S): USA

U.S. Pat. Appl. Publ., 102 pp., Cont.-in-part of U.S. SOURCE:

Ser. No. 600,862.

CODEN: USXXCO

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND DATE	APPLICATION NO.	DATE
US 2005042227	A1 20050224	US 2004-812849	20040330
US 2005026823	A1 20050203	US 2003-600862	20030620
WO 2005002515	A2 20050113	WO 2004-US19153	20040617
WO 2005002515	A3 20050714		
W: AE, AG, AL,	AM, AT, AU, AZ,	BA, BB, BG, BR, BW, BY	, BZ, CA, CH,
CN, CO, CR,	CU, CZ, DE, DK,	DM, DZ, EC, EE, EG, ES	, FI, GB, GD,
GE, GH, GM,	HR, HU, ID, IL,	IN, IS, JP, KE, KG, KP	, KR, KZ, LC,
LK, LR, LS,	LT, LU, LV, MA,	MD, MG, MK, MN, MW, MX	, MZ, NA, NI,
NO, NZ, OM,	PG, PH, PL, PT,	RO, RU, SC, SD, SE, SG	, SK, SL, SY,
TJ, TM, TN,	TR, TT, TZ, UA,	UG, US, UZ, VC, VN, YU	, ZA, ZM, ZW
RW: BW, GH, GM,	KE, LS, MW, MZ,	NA, SD, SL, SZ, TZ, UG	, ZM, ZW, AM,
AZ, BY, KG,	KZ, MD, RU, TJ,	TM, AT, BE, BG, CH, CY	, CZ, DE, DK,
EE, ES, FI,	FR, GB, GR, HU,	IE, IT, LU, MC, NL, PL	, PT, RO, SE,
SI, SK, TR,	BF, BJ, CF, CG,	CI, CM, GA, GN, GQ, GW	, ML, MR, NE,
SN, TD, TG			
PRIORITY APPLN. INFO.:		US 2003-600862	A2 20030620

The present invention is directed to a methods and compns. for receptor-mediated drug delivery, particularly across the blood-brain barrier. The present invention relates to the discovery that megalin ligands can be used as carriers or vectors for the delivery of active agents via transcytosis. RAP protein is such a ligand, which serves to increase the transport of therapeutic agents across the blood brain barrier and/or deliver agents to lysosomes of cells within and without the cental nervous system.

L22 ANSWER 13 OF 23 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:160994 CAPLUS

DOCUMENT NUMBER:

TITLE: Compositions and methods using heparin mimetics for inhibiting slit protein and glypican interactions, and

use for promoting axonal regeneration and treating

US 2004-812849

spinal cord injury

Margolis, Richard U. New York University, USA PATENT ASSIGNEE(S): PCT Int. Appl., 44 pp. SOURCE:

CODEN: PIXXD2 DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

INVENTOR(S):

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PATENT NO.
                            KIND
                                    DATE
                                                  APPLICATION NO.
                                                                              DATE
                             ----
                                                  WO 2004-US26562
     WO 2005016285
                                     20050224
                                                                              20040813
                             A2
          W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
               CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
              GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
               NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
          TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
              AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
               SN, TD, TG
PRIORITY APPLN. INFO.:
                                                   US 2003-494906P
                                                                          P 20030813
     The invention discloses a composition for inhibiting slit protein and glypican
     interactions which include an effective amount of a heparin mimetic. A
     pharmaceutical composition for inhibiting slit protein and glypican
      interactions includes an effective amount of a heparin mimetic and a
     pharmaceutical carrier. A composition for promoting axonal regeneration
     includes an effective amount of a heparin mimetic. A therapeutic composition for
     inhibiting slit protein and glypican interaction or promoting axonal
      regeneration includes an effective amount of a heparin mimetic. Also
     disclosed are various methods for inhibiting slit protein and glypican
     interaction, promoting axonal regeneration, and treating spinal cord
     injury.
L22 ANSWER 14 OF 23 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:
                             2005:34719 CAPLUS
DOCUMENT NUMBER:
                             142:141213
TITLE:
                             Delivery of therapeutic compounds to the brain and
                             other tissues through lipoprotein receptor-related
                             proteins for the treatment of CNS and lysosomal
                             storage diseases
INVENTOR(S):
                             Zankel, Todd; Starr, Christopher M.; Gabathuler,
                             Reinhard
PATENT ASSIGNEE(S):
                             Biomarin Pharmaceutical Inc., USA
SOURCE:
                             PCT Int. Appl., 192 pp.
                             CODEN: PIXXD2
DOCUMENT TYPE:
                             Patent
LANGUAGE:
                             English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:
      PATENT NO.
                            KIND DATE
                                                  APPLICATION NO.
                                                                              DATE
                             ----
     WO 2005002515
                                     20050113
                             A2
                                                   WO 2004-US19153
                                                                              20040617
     WO 2005002515
                                     20050714
                             АЗ
          W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
               CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
               GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
               LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
               NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
          TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
               AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
               SN, TD, TG
      US 2005026823
                                     20050203
                                                   US 2003-600862
                                                   US 2004-812849
     US 2005042227
                             A1
                                     20050224
                                                                              20040330
                                                                          A 20030620
PRIORITY APPLN. INFO.:
                                                   US 2003-600862
                                                   US 2004-812849
                                                                          A 20040330
```

AB The present invention is directed to a methods and compns. for receptor mediated drug delivery, particularly across the blood-brain barrier. The present invention relates to the discovery that megalin ligands can be used as carriers or vectors for the delivery of active agents via transcytosis. An exemplary such ligand is RAP, which serves to increase the transport of therapeutic and /or diagnostic/investigational agents across the blood brain barrier and/or deliver agents to lysosomes of cells within and without the CNS. In particular embodiments, RAP fusion proteins containing human glucosidase (GAA), alpha-L-iduronidase (IDU) and glial-derived neurotrophic factor (GDNF) are tested for uptake or transcytosis in bovine brain capillary endothelial cell or fibroblast cell lines for the treatment lysosomal storage diseases.

10/628.999 L22 ANSWER 15 OF 23 CAPLUS COPYRIGHT 2005 ACS on STN ACCESSION NUMBER: 2004:1156506 CAPLUS DOCUMENT NUMBER: 142:100372 Antimicrobial silver formulations comprising silver TITLE: and a silver resistance inhibitor INVENTOR(S): Trotter, Patrick; Jampani, Hanuman; Mitscher, Lester; Pillai, Segaran PATENT ASSIGNEE(S): Johnson & Johnson Medical Limited, UK SOURCE: PCT Int. Appl., 26 pp. CODEN: PIXXD2 DOCUMENT TYPE: Patent LANGUAGE: English FAMILY ACC. NUM. COUNT: PATENT INFORMATION: PATENT NO. KIND DATE APPLICATION NO. DATE WO 2004112805 20041229 WO 2004-GB2631 A1 20040621 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG GB 2402880 Α1 20041222 GB 2003-14453 20030620 A 20030620 PRIORITY APPLN. INFO.: GB 2003-14453 P 20030804 US 2003-491990P An antimicrobial composition comprising silver and at least one compound which interacts with a microbial cell wall to inhibit microbial silver resistance. The resistance inhibitors include mols. that can promote the transport of silver across the cell wall, and/or disrupt the cell wall to allow silver into the cell, and/or disrupt ion pump mechanisms in the cell wall for removing silver from the cell. Inhibitor compds. include fusaric acid, tocopherol, resveratrol, and myristic acid. Also provided are wound dressings comprising the inventive compns. REFERENCE COUNT: THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT L22 ANSWER 16 OF 23 CAPLUS COPYRIGHT 2005 ACS on STN ACCESSION NUMBER: 2004:754417 CAPLUS DOCUMENT NUMBER: 141:256532 TITLE: Soluble derivatives of human neutral hyaluronidase and their secretory manufacture for use in therapeutic modulation of glycosaminoglycan metabolism INVENTOR(S): Bookbinder, Louis H.; Kundu, Anirban; Frost, Gregory PATENT ASSIGNEE(S): Deliatroph Pharmaceuticals, Inc., USA SOURCE: PCT Int. Appl., 210 pp. CODEN: PIXXD2 DOCUMENT TYPE: Patent LANGUAGE: English FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

311 2			011.														
PAT	TENT	NO.			KIN	D	DATE			APPL:	CAT:	I NO	NO.		D	ATE	
						-											
WO	2004	0781	40		A2		2004	0916	1	NO 2	004 <b>-</b> 1	JS66	56		20	0040	305
	W:	ΑE,	ΑE,	AG,	AL,	AL,	AM,	AM,	AM,	AT,	AT,	ΑU,	ΑZ,	AZ,	BA,	BB,	BG,
		BG,	BR,	BR,	BW,	BY,	BY,	ΒZ,	BZ,	CA,	CH,	CN,	CN,	CO,	co,	CR,	CR,
		CU,	CU,	CZ,	CZ,	DE,	DE,	DK,	DK,	DM,	DZ,	EC,	EC,	EE,	EE,	EG,	ES,
		ES,	FI,	FΙ,	GB,	GD,	GE,	GE,	GH,	GM,	HR,	HR,	HU,	HU,	ID,	IL,	IN,
		IS,	JP,	JP,	ΚE,	ΚE,	KG,	KG,	ΚP,	ΚP,	ΚP,	KR,	KR,	ΚZ,	ΚZ,	ΚZ,	LC,
		LK,	LR,	LS,	LS,	LT,	LU,	LV,	MA,	MD,	MD,	MG,	MK,	MN,	MW,	MX,	MX,
		ΜZ,	ΜZ,	NA,	NI												
	RW:	BW,	GH,	GM,	ΚE,	LS,	MW,	ΜZ,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AT,	BE,
		BG,	CH,	CY,	CZ,	DE,	DK,	EE,	ES,	FI,	FR,	GB,	GR,	ΗU,	ΙE,	IT,	LU,
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		GN,	GQ,	GW,	ML,	MR,	NE,	SN,	TD,	TG,	BF,	ВJ,	CF,	CG,	CI,	CM,	GA,
		GN,	GQ,	GW,	ML,	MR,	NE,	SN,	TD,	TG							

US 2004268425 Al 20041230 US 2004-795095 20040305
PRIORITY APPLN. INFO::

US 2003-452360P P 20030305

AB A variant of human neutral active hyaluronidase with improved solubility is constructed and a cDNA encoding it is cloned for manufacture.

solubility is constructed and a cDNA encoding it is cloned for manufacture of the enzyme for use in the the treatment of glycosaminoglycan-associated pathologies. This variant of the enzyme lacks its hydrophobic C-terminal domain including the GPI anchor to improve solubility and increase yields of secreted activity. Minimally active domains of the enzyme, including asparagine-linked glycosidation required for a functional enzyme are identified. Secretory manufacture of the enzyme and the use of leader peptides that increase the efficiency of secretion of the enzyme are also described. The signal and leader peptide of the enzyme is unusually long and may play a role in limiting secretion by promoting aggregation. Replacing it with the signal peptide of the mouse Ig  $\kappa$  chain increased yields of secreted enzyme by .apprx.6-fold. Modified forms of the enzyme, e.g. sialylated and PEGylated, with increased stability and serum pharmacokinetics over naturally occurring slaughterhouse enzymes are described. Further described are suitable formulations of a substantially purified recombinant sHASEGP glycoprotein derived from a eukaryotic cell that generate the proper glycosylation required for its optimal activity.

L22 ANSWER 17 OF 23 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004

2004:354980 CAPLUS

DOCUMENT NUMBER:

140:363010

TITLE:

Taxanes covalently bounded to hyaluronic

acid or hyaluronic acid derivatives

INVENTOR(S):

De Luca, Gilda; Marini Bettolo, Rinaldo; Migneco,

Luisa Maria

PATENT ASSIGNEE(S):

Fidia Farmaceutici S.P.A., Italy

SOURCE:

PCT Int. Appl., 56 pp.

\_\_\_\_

CODEN: PIXXD2

DOCUMENT TYPE: LANGUAGE: Patent English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

	PA?	PATENT NO.					D	DATE			APPL:	ICAT:	ION	١٥.		Di	ATE	
	WO	2004	0356	29		A2	_	2004	0429	,	WO 2	003-	EP11	239		20	0031	010
	WO	2004	0356	29		А3		2004	0624									
	WO	2004	0356	29		C1		2005	0609									
	WO	2004	0356	29		C2		2005	0707									
		W:	ΑE,	AG,	AL,	AM,	AT,	ΑU,	AZ,	BA,	BB,	BG,	BR,	BY,	BZ,	CA,	CH,	CN,
			co,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	EG,	ES,	FI.	GB,	GD,	GE,
								IL.						-				
			LR,	LS,	LT,	LU,	LV,	MA.	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NI,	NO,	NZ,
			OM,	PG,	PH,	PL,	PT,	RO,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	SY,	TJ,	TM,
								UG,										
		RW:						MZ,									AZ,	BY,
			KG,	KZ,	MD,	RU,	TJ,	TM,	AT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,	EE,	ES,
			FI,	FR,	GB,	GR,	HU,	IE,	IT,	LU,	MC,	NL,	PT,	RO,	SE,	SI,	SK,	TR,
			BF,	ВJ,	CF,	CG,	CI,	CM,	GA,	GN,	GQ,	GW,	ML,	MR,	NE,	SN,	TD,	TG
	CA	2502						2004										
	EP	1560	854			A2		2005	0810		EP 2	003-	7481	26		2	0031	010
		R:	ΑT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	IT,	LI,	LU,	NL,	SE,	MC,	PT,
								RO,										
	BR 2003015431					A		2005	0816	-	BR 2	003-	1543	1	-	2	0031	010
PRIO	IORITY APPLN. INFO.:										IT 2	002-	PD27	1		A 2	0021	018
	ONTIT ALLBO.										WO 2	003-	EP11	239	1	W 2	0031	010
				_			_					_	_					

Water-soluble taxanes covalently bounded to hyaluronic acid or hyaluronic acid derivs., and in particular to paclitaxel and docetaxel, are useful for the preparation of pharmaceutical compns. to be used in the field of oncol., in the treatment of autoimmune disorders and of restenosis. The invention also relates to the process for preparing taxanes covalently bounded to hyaluronic acid or hyaluronic acid derivs. by direct synthesis between mols. of hyaluronic acid and of taxane or by indirect synthesis by the introduction of a spacer between the hyaluronic acid or hyaluronic acid derivative and the taxane. Ester derivative of HA covalently bound to paclitaxel with 16% of esterification of the carboxyl was prepared Effect of the ester derivative of HA with paclitaxel in nude mouse after implantation of human ovary adenocarcinoma cells, was studied. The control animals developed adenocarcinoma of the ovary and died between 15 and 75th days after inoculation of the cancer cells. On the 92nd day after intervention, none of the animals that had received pharmacol. treatment with paclitaxel or the hyaluronate ester had died.

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L22 ANSWER 18 OF 23 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:
                           2004:80180 CAPLUS
                           140:133849
DOCUMENT NUMBER:
TITLE:
                           Particles coated on the surface with
                           hyaluronan or one of its derivatives, and
                           their use as biological vectors
                           Dellacherie, Edith; Leonard, Michele; Gref, Ruxandra;
INVENTOR(S):
                           Netter, Patrick; Payan, Elisabeth
                           Centre National de la Recherche Scientifique CNRS, Fr.
PATENT ASSIGNEE(S):
                           Fr. Demande, 20 pp.
SOURCE:
                           CODEN: FRXXBL
DOCUMENT TYPE:
                           Patent
                           French
LANGUAGE:
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
     PATENT NO.
                           KIND
                                   DATE
                                                APPLICATION NO.
                                                                          DATE
                           ----
                                                                          _____
     FR 2842737
                                   20040130
                                                FR 2002-9436
                                                                          20020725
     CA 2493470
                            AA
                                   20040219
                                                CA 2003-2493470
                                                                          20030721
     WO 2004014347
                                   20040219
                                                WO 2003-FR2299
                                                                          20030721
                            A1
         W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
              CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
              LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
              PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,
              TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
              FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
                                  20050427
                                                EP 2003-769524
                                                                          20030721
     EP 1524970
                           A1
         R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
                                                                   A 20020725
                                                FR 2002-9436
                                                WO 2003-FR2299
                                                                      W 20030721
    Particles with cores comprising an organosol. biodegradable polymer coated
     at least partially on the surface, with hyaluronan or one of its
     derives, are used as biol, vectors for active materials. Polylactide
     particles were coated with C18 alkyl derivs. of sodium hyaluronate
      . Effects of the particles on the proliferation of cultured chondrocytes
     was studied.
REFERENCE COUNT:
                           5
                                  THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS
                                  RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
L22 ANSWER 19 OF 23 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:
                           2003:989927 CAPLUS
DOCUMENT NUMBER:
                           140:19891
TITLE:
                           Compositions for treatment of diseases arising from
                           secretion of mast cell biochemicals
INVENTOR(S):
                           Theoharides, Theoharis C.
PATENT ASSIGNEE(S):
                           USA
SOURCE:
                           U.S. Pat. Appl. Publ., 8 pp., Cont.-in-part of U.S.
                           Ser. No.773,576.
                           CODEN: USXXCO
DOCUMENT TYPE:
                           Patent
LANGUAGE:
                           Enalish
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
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PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003232100	A1	20031218	US 2003-439301	20030516
US 6689748	B1	20040210	US 1998-56707	19980408
PRIORITY APPLN. INFO.:			US 1998-56707	A3 19980408
			US 2001-773576	A2 20010202

Compns. for treatment of diseases arising from products secreted by activated tissue mast cells, composed of, as active ingredients, unprocessed olive kernel (pit) extract that increases absorption of these compns. in various routes of administration, and one or more of a heavily sulfated, non-bovine proteoglycan such as shark cartilage chondroitin sulfate C, a hexosamine sulfate such as D-glucosamine sulfate, a flavonoid such as quercetin, S-adenosylmethionine, a histamine-1 receptor antagonist, a histamine-3 receptor agonist, a CRH antagonist, caffeine, fragments of myelin basic protein, rutin, polyunsatd. fatty acids, Bitter

Willow Extract and a polyamine.

L22 ANSWER 20 OF 23 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

2003:173470 CAPLUS

DOCUMENT NUMBER:

138:198677

TITLE:

Use of hyaluronan as a protective agent in chemotherapy for improved therapeutic

protocols

INVENTOR(S): PATENT ASSIGNEE(S):

Brown, Tracey Jean; Fox, Richard Mark Meditech Research Limited, Australia

SOURCE:

PCT Int. Appl., 96 pp.

CODEN: PIXXD2 Patent

DOCUMENT TYPE: LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PA'	TENT	NO.			KIN	D .	DATE		•		ICAT:				D.	ATE	
WO	2003	0180	62		A1		2003	0306	1	WO 2	002-	AU11	60		2	0020	827
	W:										BG,						
		co,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	ES,	FI,	GB,	GD,	GE,	GH,
		GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,	KP,	KR,	KZ,	LC,	LK,	LR,
		LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NO,	NZ,	OM,	PH,
		PL,	PT,	RO,	RU,	SD,	SE,	SG,	SI,	SK,	SL,	TJ,	TM,	TN,	TR,	TT,	TZ,
											ZW,						
			TJ,		•	•	•	•	•	•	•	•	•	•	•	•	•
	RW:	GH,	GM,	KE,	LS.	MW.	MZ.	SD,	SL,	SZ,	TZ,	UG,	ZM.	ZW.	AT,	BE.	BG.
		CH,	CY,	CZ,	DE,	DK,	EE,	ES,	FI,	FR,	GB,	GR,	IE,	IT,	LU,	MC,	NL.
		PT,	SE,	SK,	TR,	BF,	BJ,	CF,	CG,	CI,	CM,	GA,	GN,	GQ,	GW,	ML,	MR,
		NE,	SN,	TD,	TG		-				-	-	-		-	-	•
CA	2458	856			AΑ		2003	0306		CA 2	002-	2458	856		2	0020	827
EP	1427	447			A1		2004	0616		EP 2	002-	7598	88		2	0020	827
	R:	ΑT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	IT,	LI,	LU,	NL,	SE,	MC,	PT,
		ΙE,	SI,	LT,	LV,	FI,	RO,	MK,	CY,	AL,	TR,	BG,	CZ,	EE,	SK		
JP	2005	5055	40		Т2		2005	0224		JP 2	003-	5225	77		2	0020	827
US	US 2005042303				Al		2005	0224	1	US 2	004-	4799	34		2	0040	930
PRIORIT	PRIORITY APPLN. INFO.:			.:						AU 2	001-	7302			A 2	0010	827
										AU 2	001-	9504			A 2	0011	213
									1	WO 2	002-	AU11	60	1	w 2	0020	827

The invention relates to the field of chemotherapy of diseases, e.g. cell proliferation disorders including cancer. In particular, the invention discloses the use of hyaluronan (HA) as a protective agent in the treatment of subjects. HA is administered in conjunction with a chemotherapeutic agent to facilitate the prolonged administration of a dose of the chemotherapeutic agent to be administered to a subject. Owing to the protective effects of the HA, the dose of chemotherapeutic agent may be substantially higher than a generally accepted ED, which would otherwise be expected to cause unacceptable side effects in the subject.

REFERENCE COUNT:

THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 21 OF 23 CAPLUS COPYRIGHT 2005 ACS on STN

4

ACCESSION NUMBER:

2002:711276 CAPLUS

DOCUMENT NUMBER:

137:237738

TITLE:

Pharmaceutical compositions for buccal and pulmonary administration comprising an alkali metal alkyl sulfate and at least three micelle-forming compounds

Modi, Pankaj

INVENTOR(S): PATENT ASSIGNEE(S):

Generex Pharmaceuticals Incorporated, Can.

SOURCE:

U.S., 11 pp., Cont.-in-part of U.S. Ser. No. 519,285. CODEN: USXXAM

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

PATEN	IT NO.	KIND	DATE	APPLICATION NO.	DATE
US 64	51286	B1	20020917	US 2000-574504	20000519
US 64	136367	B1	20020820	US 1999-251464	19990217
US 63	312665	B1	20011106	US 1999-386284	19990831
US 63	375975	B1	20020423	US 2000-519285	20000306
CA 24	10065	AA	20011122	CA 2001-2410065	20010507
WO 20	01087268	A1	20011122	WO 2001-CA661	20010507

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W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
               HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
               LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU,
               ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
          RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
               BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
                                      20030402
                                                    EP 2001-931281
                                                                                20010507
     EP 1296648
                              A1
          R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
               IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
     NZ 522524
                              Α
                                      20030725
                                                    NZ 2001-522524
     JP 2003533469
                              T2
                                      20031111
                                                    JP 2001-583737
                                                                                20010507
     US 2003035831
                                      20030220
                                                    US 2002-222699
                                                                                20020816
                              Αl
     US 6849263
                              B2
                                      20050201
     US 2003157029
                                      20030821
                                                    US 2002-222240
                                                                                20020816
PRIORITY APPLN. INFO.:
                                                    US 1998-113239P
                                                                            P 19981221
                                                    US 1999-251464
                                                                            A2 19990217
                                                    US 1999-386284
                                                                            A2 19990831
                                                    US 2000-519285
                                                                            A2 20000306
                                                    US 2000-574504
                                                                            A 20000519
                                                    WO 2001-CA661
                                                                            W 20010507
     Pharmaceutical compns. comprising a macromol. pharmaceutical agent in
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mixed micellar form are disclosed. The mixed micelles are formed from an alkali metal alkyl sulfate, and at least three different micelle-forming compds. Micelle size ranges between about 1 and 10 nm. Methods for making and using the compns. are also disclosed. A preferred method for administering the present composition is through the buccal region of the mouth. For example, to 1000 mg of powdered insulin dissolved in 10 mL of distilled water were added 50 mg sodium lauryl sulfate, 36 mg deoxycholate, 50 mg trihydroxyoxocholanylglycine (sodium glycocholate) and 20 mg dibasic Na phosphate followed by 250 mg glycerin, 40 mg m-cresol and 40 mg phenol. The solution (1 mL) was pipetted into 10 mL capacity glass vials, the vials were charged with HFA-134a propellant and stored at room temperature. The oral insulin composition prepared (70 unit dose) performed much better in diabetic patients than hypoglycemic Metformin tablets in controlling glucose levels.

REFERENCE COUNT:

THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS 36 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 22 OF 23 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:151474 CAPLUS

DOCUMENT NUMBER: 136:205405

TITLE:

Mixed micellar drug delivery system and method of

preparation

INVENTOR(S): Modi, Pankaj

PATENT ASSIGNEE(S): Generex Pharmaceuticals Incorporated, Can.

SOURCE: U.S., 12 pp., Cont.-in-part of U.S. Ser. No. 386,285.

CODEN: USXXAM

DOCUMENT TYPE: Patent LANGUAGE: Enalish

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE			
US 6350458	B1	20020226	US 2000-543988	20000406			
US 6017545	Α	20000125	US 1998-21114	19980210			
US 6231882	B1	20010515	US 1998-216733	19981221			
US 6221378	B1	20010424	US 1999-386285	19990831			
PRIORITY APPLN. INFO.:			US 1998-21114 A	2 19980210			
			US 1998-216733 A	2 19981221			
			US 1999-386285 A	2 19990831			

Pharmaceutical compns. comprising a macromol. pharmaceutical agent in micellar form are disclosed. The micelles are formed from an alkali metal alkyl sulfate, and at least one addnl. micelle-forming compound as described in the specification. An alkali metal salicylate and a pharmaceutically acceptable edetate are also included in the composition Micelle size ranges between about 1 and 10 nm. Methods for making and using the compns. are also disclosed. A buffer solution was prepared using  $0.5\ g$  sodium lauryl sulfate, 0.5 g sodium salicylate, and 0.25 g disodium edetate dissolved in 10 mL of water. The solution was added to 16 mg (400 units) of insulin and mixed, to form micellar insulin. Sep., 100 mg of powdered Phosphatidylcholine-H was added to a glass beaker and to this powder was added 10 mL 50% ethanol. This solution was then added to the above buffer

solution, to give a 30 units/mg insulin solution, with vigorous mixing to form a mixed micellar solution To this was added 0.6 mL of sodium hyaluronate and 0.2 mL of 2% menthol solution containing 3% sorbitol. Type II diabetic human volunteers took the micellar insulin orally. The oral insulin at a dosage of three times higher than the injected level, was comparable to the injected insulin.

REFERENCE COUNT:

13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 23 OF 23 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

1999:292567 CAPLUS

DOCUMENT NUMBER:

130:329203

TITLE:

Drug composition with controlled drug release rate

comprising hyaluronate and biodegradable

polymers

INVENTOR(S):

Suzuki, Makoto; Ishigaki, Kenji; Okada, Minoru; Ono,

Kenji; Kasai, Shuichi; Imamori, Katsumi

PATENT ASSIGNEE(S):

SSP Co., Ltd., Japan Eur. Pat. Appl., 19 pp.

SOURCE:

CODEN: EPXXDW

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

	PAT	ENT	NO.			KIN	)	DATE		API	PLIC	ATI	ON 1	١٥.		Di	ATE	
							-									-		
	EΡ	9131	49			A1		1999	0506	EP	199	8-1	1943	15		1:	9981	014
	EΡ	9131	49			B1		2005	0309									
		R:	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB, GF	₹, I	Т,	LI,	LU,	NL,	SE,	MC,	PT,
			ΙE,	SI,	LT,	LV,	FI,	RO										
	JΡ	1113	0697			A2		1999	0518	JP	199	7-2	9400	38		1	9971	027
	WT	5202	92			В		2003	0211	TW	199	8-8	711	6892		1	9981	012
	US	6375	988			B1		2002	0423	US	199	8-1	722	70		1:	9981	014
	CA	2251	281			AΑ		1999	0427	CA	199	8-2	2513	281		1	9981	020
	CN	1220	874			Α		1999	0630	CN	199	8-1	226	L 4		1	9981	027
	НK	1019	142			A1		2004	0716	HK	199	9-1	0438	32		1:	9991	007
RIOR	ITY	APP	LN.	INFO	.:					JP	199	7-2	9400	3C	1	1	9971	027

AΒ A drug composition with a controlled drug release rate is disclosed. The drug composition comprises (a) a biodegradable, biocompatible high-mol. substance and/or polyvalent metal ions or polyvalent metal ion source, and (b) hyaluronic acid or a salt thereof; and a drug incorporated as an ingredient (c) in said matrix. The drug composition has biodegradability and biocompatibility, permits easy control of a release rate of the drug, and can persistently exhibit its pharmacol. effect over a long time. A solution of 1% sodium hyaluronate (I) was added to 200 mg medium-chain fatty acid triglyceride and the mixture was stirred followed by addition of 50% aqueous calcium chloride solution The microspheres thus obtained were separated, washed, and dried. The microspheres had an average particle size of 78.4 μm and I content of 78.1%. 12

REFERENCE COUNT:

THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT